PHARMACEUTICAL USES FOR ALPHA2DELTA LIGANDS

This application claims priority from U.S. Provisional Application 60/425,219 filed November 8, 2002; the entire contents of which are hereby incorporated herein by reference.

This invention relates to methods of treating various central nervous system and other disorders by administering a compound that exhibits activity as an alpha2delta ligand ($\alpha 2\delta$ ligand). Such compounds have affinity for the $\alpha 2\delta$ subunit of a calcium channel. Such compounds have also been referred to in the literature as gamma-aminobutyric acid (GABA) analogs.

BACKGROUND OF THE INVENTION

Several alpha2delta ligands are known. Gabapentin, a cyclic alpha2delta ligand, is now commercially available (Neurontin®, Warner-Lambert Company) and extensively used clinically for treatment of epilepsy and neuropathic pain. Such cyclic alpha2delta ligands are described in US Patent No. 4,024,175, which issued on May 17, 1977, and US Patent No. 4,087,544, which issued on May 2, 1978. Other series of alpha2delta ligands are described in US Patent No. 5,563,175, which issued on October 8, 1996, US Patent No. 6,316,638, which issued on November 13, 2001, US Provisional Patent Application 60/353,632, which was filed on January 31, 2002, European Patent Application EP 1112253, which was published on July 4, 2001, PCT Patent Application WO 99/08671, which was published on February 25, 1999, and PCT Patent Application WO 99/61424, which was published on December 2, 1999. These patents and applications are incorporated herein by reference in their entireties.

SUMMARY OF THE INVENTION

This invention relates to a method of treating a disorder or condition selected from faintness attacks, epilepsy, asphyxia, general anoxia,

hypoxia, spinal cord trauma, traumatic brain injury, head trauma, cerebral ischemia, stroke (including thromboembolic stroke, focal ischemia, global ischemia, transient cerebral ishemia attacks and other cerebral vascular problems accompanied by cerebral ischemia such as in patients undergoing carotid endarterectomy or other vascular surgical procedures in general or diagnostic vascular surgical procedures such as angiography), cramp caused by thiosemicarbazide, cardiazole cramp, and cerebral vascular disorders due to acute or chronic cerebrovascular damage such as cerebral infarction, subarachnoid haemorrhage or cerebral oedema in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of neurocardiac disorders such as neurocardiac syncope, neurogenic syncope, hypersensitive Carotid sinus, neurovascular syndrome and arrythmias including arrythmias secondary to gastrointestinal disturbances in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from acute pain, chronic pain, pain resulting from soft tissue and peripheral damage such as acute trauma; postherpetic neuralgia, occipital neuralgia, trigeminal neuralgia, segmental or intercostal neuralgia and other neuralgias; pain associated with osteoarthritis and rheumatoid arthritis; musculo-skeletal pain such as pain associated with strains, sprains and trauma such as broken bones; spinal pain, central nervous system pain such as pain due to spinal cord or brain stem damage; lower back pain, sciatica, dental pain, myofascial pain syndromes, episiotomy pain, gout pain, and pain resulting from burns; deep and visceral pain, such as heart pain; muscle pain, eye pain, inflammatory pain, orofacial pain, for example, odontalgia; abdominal pain, and gynecological pain, for example, dysmenorrhoea, labour pain and pain

associated with endometriosis; somatogenic pain; pain associated with nerve and root damage, such as pain associated with peripheral nerve disorders, for example, nerve entrapment and brachial plexus avulsions; pain associated with limb amputation, tic douloureux, neuroma, or vasculitis; diabetic neurapathy, chemotherapy-induced-neuropathy, acute herpetic and postherpetic neuralgia; atypical facial pain, neuropathic lower back pain, and arachnoiditis, trigeminal neuralgia, occipital neuralgia, segmental or intercostal neuralgia, HIV related neuralgias and AIDS related neuralgias and other neuralgias; allodynia, hyperalgesia, burn pain, idiopathic pain, pain caused by chemotherapy; occipital neuralgia, psychogenic pain, brachial plexus avulsion, pain associated with restless legs syndrome; pain associated with gallstones; pain caused by chronic alcoholism or hypothyroidism or uremia or vitamin deficiencies; neuropathic and non-neuropathic pain associated with carcinoma, often referred to as cancer pain, phantom limb pain, functional abdominal pain, headache, including migraine with aura, migraine without aura and other vascular headaches, acute or chronic tension headache, sinus headache and cluster headache; temperomandibular pain and maxillary sinus pain; pain resulting from ankylosing spondylitis; pain caused by increased bladder contractions; post operative pain, scar pain, and chronic non-neuropathic pain such as pain associated with HIV, anthralgia, vasculitis and fibromyalgia in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from mood disorders, such as depression, or more particularly, depressive disorders, for example, major depressive disorder, severe unipolar recurrent major depressive episodes, dysthymic disorder, depressive neurosis and neurotic depression, melancholic depression including anorexia, weight loss, insomnia, early morning waking or psychomotor retardation, atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability; treatment resistant depression; seasonal affective disorder and

pediatric depression; premenstrual syndrome, premenstrual dysphoric disorder, hot flashes, bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II disorder and cyclothymic disorder; seasonal affective disorder, conduct disorder and disruptive behavior disorder; stress related somatic disorders and anxiety disorders, such as panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobias (*e.g.*, specific animal phobias), social anxiety disorder, social phobia, obsessive-compulsive disorder, stress disorders including post-traumatic stress disorder and acute stress disorder, and generalized anxiety disorder in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of borderline personality disorder; schizophrenia and other psychotic disorders, for example, schizophreniform disorders, schizoaffective disorders, delusional disorders, brief psychotic disorders, shared psychotic disorders, psychotic disorders due to a general medical condition, psychotic disorders with delusions or hallucinations, substance induced psychotic disorder, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders such as severe major depressive disorder; mood disorders associated with psychotic disorders such as acute mania and depression associated with bipolar disorder, mood disorders associated with schizophrenia; and behavioral disturbances associated with mental retardation in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of sleep disorders such as insomnia (*e.g.,* primary insomnia including psychophysiological and idiopathic insomnia, secondary insomnia including insomnia secondary to restless legs syndrome, Parkinson's disease or another chronic disorder, and transient insomnia), somnambulism, sleep deprivation, REM sleep

disorders, sleep apnea, hypersomnia, parasomnias, sleep-wake cycle disorders, jet lag, narcolepsy, sleep disorders associated with shift work or irregular work schedules, deficient sleep quality due to a decrease in slow wave sleep caused by medications or other sources, and other sleep disorders in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of increasing slow wave sleep and increasing growth hormone secretion in a human subject comprising administering to a human subject in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of respiratory diseases, particularly those associated with excess mucus secretion, such as chronic obstructive airways disease, bronchopneumonia, chronic bronchitis, cystic fibrosis, adult respiratory distress syndrome, and bronchospasm; cough, whooping cough, angiotensin converting enzyme (ACE) induced cough, pulmonary tuberculosis, allergies such as eczema and rhinitis; contact dermatitis, atopic dermatitis, urticaria, and other eczematoid dermatitis; itching, hemodialysis associated itching; inflammatory diseases such as inflammatory bowel disease, psoriasis, osteoarthritis, cartilage damage (*e.g.*, cartilage damage resulting from physical activity or osteoarthritis), rheumatoid arthritis, psoriatic arthritis, asthma, pruritis and sunburn; and hypersensitivity disorders such as poison ivy in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of neurodegenerative disorders, such as Parkinson's disease (PD), Huntington's disease (HD) and Alzheimer's disease (AD); delerium, dementias (*e.g.,* senile dementia of the Alzheimer's type, senile dementia, vascular dementia, HIV-1

associated dementia, AIDS dementia complex (ADC), dementias due to head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, or due to multiple etiologies), amnestic disorders, other cognitive or memory disorders, and behavioral symptoms of dementia in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of Down's syndrome; Sjogren's syndrome, hypertension, hematopoiesis, postoperative neuroma, benign prostatic hypertrophy, periodontal disease, hemorrhoids and anal fissures, infertility, reflex sympathetic dystrophy, hepatitis, tenalgia attendant to hyperlipidemia, vasodilation, fibrosing and collagen diseases such as scleroderma and eosinophilic fascioliasis; and vasospastic diseases such as angina, migraine and Reynaud's disease in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of ophthalmic diseases such as dry eye syndrome, conjunctivitis, vernal conjunctivitis, and the like; and ophthalmic conditions associated with cell proliferation such as proliferative vitreoretinopathy in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of autism, attention deficit hyperactivity disorder (ADHD), angiogenesis (*i.e.,* use for the inhibition of angiogenesis), Reiter's syndrome and anthropathies in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of substance-related disorders arising from the use of alcohol, amphetamines (or amphetamine-like substances) caffeine, cannabis, cocaine, hallucinogens, inhalants and aerosol propellants, nicotine, opioids, phenylglycidine derivatives, sedatives, hypnotics, and anxiolytics, which substance-related disorders include dependence and abuse, intoxication, withdrawal, intoxication delerium and withdrawal delerium; and addiction disorders involving addictions to behaviors (*e.g.*, addictions to gambling and other addictive behaviors) in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of Down's syndrome; demyelinating diseases such as multiple sclerosis (MS) and amylolateral sclerosis (ALS) in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of pervasive development disorder, fibromyalgia, human immunodeficiency virus (HIV) infections; HIV encephalopathy; dissociative disorders such as body dysmorphic disorders; eating disorder such as anorexia and bulimia; ulcerative colitis; Crohn's disease; irritable bowel syndrome; chronic pancreatitis, chronic fatigue syndrome; sudden infant death syndrome (SIDS); overactive bladder; lower urinary tract symptoms of overactive bladder; chronic cystitis; chemotherapy induced cystitis; cough, angiotensin converting enzyme (ACE) induced cough, itch, hiccups, premenstrual syndrome, premenstrual dysphoric disorder, amenorrheic disorders such as desmenorrhea; reflex sympathetic dystrophy such as shoulder/hand syndrome; plasma extravasation resulting from cytokine chemotherapy; disorders of bladder function such as chronic cystitis, bladder detrusor hyper-reflexia, inflammation of the urinary tract and urinary incontinence, including urinary urge incontinence,

overactive bladder, stress incontinence and mixed incontinence; fibrosing and collagen diseases such as scleroderma and eosinophilic fascioliasis; blood flow disorders caused by vasodilation and vasospastic diseases such as angina and Reynaud's disease; sexual dysfunctions including premature ejaculation and male erectile dysfunction in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of movement disorders such as primary movement disorders, akinesias, dyskinesias (*e.g.*, familial paroxysmal dyskinesia, tardive dyskinesia, tremor, chorea, myoclonus, tics and other dyskinesias) spasticities, Tourette's syndrome, Scott syndrome, palsys (*e.g.*, Bell's palsy, cerebral palsy, birth palsy, brachial palsy, wasting palsy, ischemic palsy, progressive bulbar palsy and other palsys), akinetic-rigid syndrome; extra-pyramidal movement disorders such as medication-induced movement disorders, for example, neuroleptic-induced Parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremour; restless legs syndrome and movement disorders associated with Parkinson's disease or Huntington's disease in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of mastalgia syndromes, motion sickness, systemic lupus erythematosis and immune dysfunctions (*e.g.*, stress induced immune dysfunctions such as idiopathic immune dysfunctions, post infection immune dysfunctions, post lumpectomy immune dysfunctions, porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs) in a mammal, comprising administering to a mammal in need of such treatment a

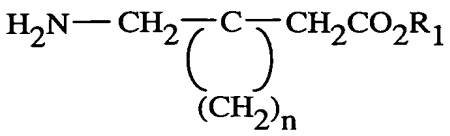
therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of gastrointestinal (GI) disorders, including inflammatory gastrointestinal disorders such as inflammation bowel disease, disorders caused by *helicobacter pylori* and diseases of the GI tract such as gastritis, proctitis, gastroduodenal ulcers, peptic ulcers, dyspepsia, disorders associated with the neuronal control of viscera, ulcerative colitis, Crohn's disease, irritable bowel syndrome and emesis, including post operative nausea and post operative vomiting, and including acute, delayed or anticipatory emesis (emesis includes emesis induced by chemotherapy, radiation, toxins, viral or bacterial infections, pregnancy, vestibular disorders, for example, motion sickness, vertigo, dizziness and Meniere's disease, surgery, migraine, variations in intercranial pressure, gastro-oesophageal reflux disease, acid indigestion, over indulgence in food or drink, acid stomach, waterbrash or regurgitation, heartburn, for example, episodic, nocturnal or meal-induced heartburn, and dyspepsia) in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

This invention also relates to a method of treating a disorder or condition selected from the group consisting of neoplasms, including breast tumours, gastric carcinomas, gastric lymphomas, neuroganglioblastomas and small cell carcinomas such as small cell lung cancer in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of an alpha2delta ligand or a pharmaceutically acceptable salt thereof.

The foregoing methods are also referred to herein, collectively, as the "invention methods".

Preferred embodiments of the invention methods utilize an alpha2delta ligand that is a cyclic amino acid compound of Formula I

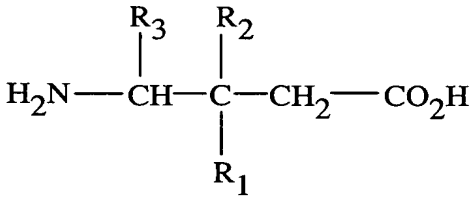


I

wherein R_1 is hydrogen or lower alkyl and n is an integer of from 4 to 6, and the pharmaceutically acceptable salts thereof. An especially preferred embodiment utilizes a compound of Formula I where R_1 is hydrogen and n is 5, which compound is 1-(aminomethyl)-cyclohexane acetic acid, known generically as gabapentin. Other preferred alpha2delta ligands, or a pharmaceutically acceptable salt thereof, are compounds of Formula I wherein the cyclic ring is substituted, for example with alkyl such as methyl or ethyl. Typical of such compounds include (1-aminomethyl-3-methylcyclohexyl) acetic acid, (1-aminomethyl-3-methylcyclopentyl) acetic acid, and (1-aminomethyl-3,4-dimethylcyclopentyl) acetic acid.

The cyclic amino acids of Formula I and methods of synthesizing them are described in US Patent No. 4,024,175 and US Patent No. 4,087,544, which are both incorporated herein by reference in their entireties.

In other preferred embodiments, the invention methods utilize an alpha2delta ligand of Formula II



II

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is a straight or branched unsubstituted alkyl of from 1 to 6 carbon atoms, unsubstituted phenyl, or unsubstituted cycloalkyl of from 3 to 6 carbon atoms;

R_2 is hydrogen or methyl; and

R_3 is hydrogen, methyl, or carboxyl.

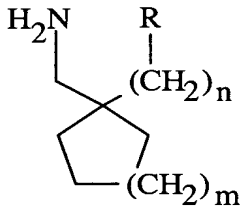
Diastereomers and enantiomers of compounds of Formula II can be utilized in the invention methods.

Preferred embodiments of the invention methods utilize a compound of Formula II that is 3-aminomethyl-5-methyl-hexanoic acid or, especially, (S)-3-(aminomethyl)-5-methylhexanoic acid, which is known generically as pregabalin.

Other preferred embodiments of the invention methods utilize a compound of Formula II that is 3-(1-aminoethyl)-5-methylheptanoic acid or 3-(1-aminoethyl)-5-methylhexanoic acid.

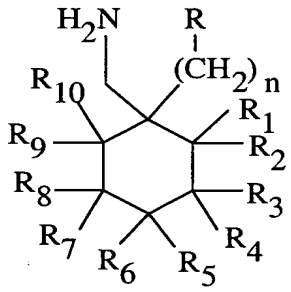
Alpha2delta ligands having the Formula II, and the synthesis of such compounds, are described in US Patent 5,563,175, which is incorporated herein by reference in its entirety.

Other preferred embodiments of the invention methods utilize an alpha2delta ligand that is a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH



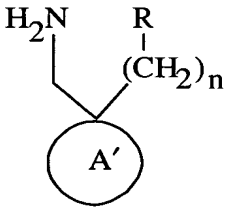
III

or



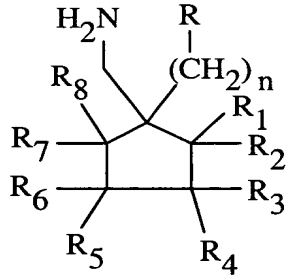
IIIC

or



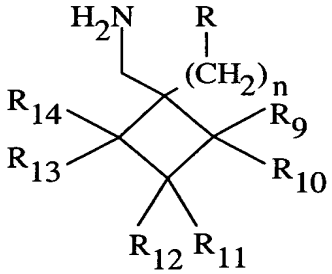
IIIF

or



IIIG

or



IIIH

or a pharmaceutically acceptable salt thereof wherein:

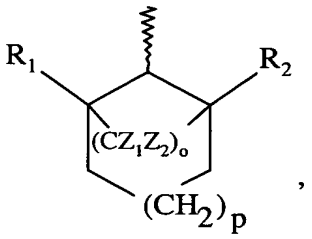
n is an integer of from 0 to 2;

m is an integer of from 0 to 3;

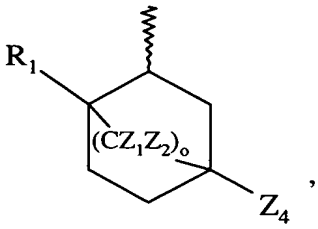
R is sulfonamide,
amide,
phosphonic acid,
heterocycle,
sulfonic acid, or
hydroxamic acid;
with the proviso that R can not be sulfonic acid when m is 2 and n is 1;

R_1 to R_{14} are each independently selected from hydrogen or straight or branched alkyl of from 1 to 6 carbons, unsubstituted or substituted benzyl or phenyl which substituents are selected from halogen, alkyl, alkoxy, hydroxy, carboxy, carboalkoxy, trifluoromethyl, and nitro;

A′ is a bridged ring selected from



(1)



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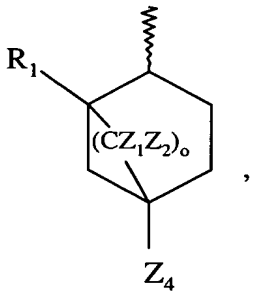

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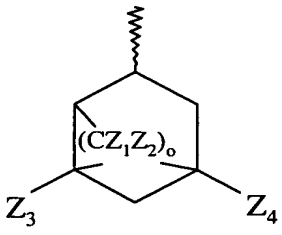

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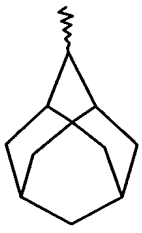


(5)

wherein

 is the point of attachment;

Z_1 to Z_4 are each independently selected from hydrogen and methyl;

o is an integer of from 1 to 4; and

p is an integer of from 0 to 2.

Other preferred embodiments of the invention methods utilize a compound selected from the following compounds of the Formula III, IIIC, IIIF, IIIG, or IIIH and their pharmaceutically acceptable salts:

(1-Aminomethyl-cyclohexylmethyl)-phosphonic acid;

(1R-trans)(1-Aminomethyl-3-methyl-cyclohexylmethyl)-phosphonic acid;

(trans)(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-phosphonic acid;

(1R-trans)(1-Aminomethyl-3-methyl-cyclopentylmethyl)-phosphonic acid;

(1S-cis)(1-Aminomethyl-3-methyl-cyclopentylmethyl)-phosphonic acid;

(1S-trans)(1-Aminomethyl-3-methyl-cyclopentylmethyl)-phosphonic acid;

(1R-cis)(1-Aminomethyl-3-methyl-cyclopentylmethyl)-phosphonic acid;

(1α,3α,4α)(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-phosphonic acid;

(1α,3β,4β)(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-phosphonic acid;

(R)(1-Aminomethyl-3,3-dimethyl-cyclopentylmethyl)-phosphonic acid;

(S)(1-Aminomethyl-3,3-dimethyl-cyclopentylmethyl)-phosphonic acid;

(1-Aminomethyl-3,3-dimethyl-cyclobutylmethyl)-phosphonic acid;

2-(1-Aminomethyl-cyclohexyl)-N-hydroxy-acetamide;

(1S-trans)2-(1-Aminomethyl-3-methyl-cyclohexyl)-N-hydroxy-acetamide;

(trans)2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-N-hydroxy-acetamide;

(1S-cis)2-(1-Aminomethyl-3-methyl-cyclopentyl)-N-hydroxy-acetamide;

(1R-trans)2-(1-Aminomethyl-3-methyl-cyclopentyl)-N-hydroxy-acetamide;

(1R-cis)2-(1-Aminomethyl-3-methyl-cyclopentyl)-N-hydroxy-acetamide;

(1S-trans)2-(1-Aminomethyl-3-methyl-cyclopentyl)-N-hydroxy-acetamide;

(1α,3α,4α)2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-N-hydroxy-acetamide;

(1α,3β,4β)2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-N-hydroxy-acetamide;

(S)2-(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-N-hydroxy-acetamide;

(R)2-(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-N-hydroxy-acetamide;

2-(1-Aminomethyl-3,3-dimethyl-cyclobutyl)-N-hydroxy-acetamide;

N-[2-(1-Aminomethyl-cyclohexyl)-ethyl]-methanesulfonamide;

(1S-cis)N-[2-(1-Aminomethyl-3-methyl-cyclohexyl)-ethyl]-methanesulfonamide;

(trans)N-[2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-ethyl]-methanesulfonamide;

(1S-cis)N-[2-(1-Aminomethyl-3-methyl-cyclopentyl)-ethyl]-methanesulfonamide;

(1R-trans)N-[2-(1-Aminomethyl-3-methyl-cyclopentyl)-ethyl]-methanesulfonamide;

(1R-cis)N-[2-(1-Aminomethyl-3-methyl-cyclopentyl)-ethyl]-methanesulfonamide;

(1S-cis)N-[2-(1-Aminomethyl-3-methyl-cyclopentyl)-ethyl]-methanesulfonamide;

(1α,3α,4α)N-[2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-ethyl]-methanesulfonamide;

(1α,3β,4β)N-[2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-ethyl]-methanesulfonamide;

(S)N-[2-(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-ethyl]-methanesulfonamide;

(R)N-[2-(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-ethyl]-methanesulfonamide;

N-[2-(1-Aminomethyl-3,3-dimethyl-cyclobutyl)-ethyl]-methanesulfonamide;

(1S-cis)3-(1-Aminomethyl-3-methyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(trans)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(1S-cis)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(1R-trans)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(1R-cis)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(1S-trans)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(1α,3α,4α)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(1α,3β,4β)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(S)3-(1-Aminomethyl-3,3-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(R)3-(1-Aminomethyl-3,3-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

3-(1-Aminomethyl-3,3-dimethyl-cyclobutylmethyl)-4H-[1,2,4]oxadiazol-5-one;

3-(1-Aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(1S-cis)3-(1-Aminomethyl-3-methyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(trans)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(1S-cis)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(1R-trans)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(1R-cis)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(1S-trans)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(1α,3α,4α)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(1α,3β,4β)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(S)3-(1-Aminomethyl-3,3-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

(R)3-(1-Aminomethyl-3,3-dimethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

3-(1-Aminomethyl-3,3-dimethyl-cyclobutylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

C-[1-(1H-Tetrazol-5-ylmethyl)-cyclohexyl]-methylamine;

(1S-cis)C-[3-Methyl-1-(1H-tetrazol-5-ylmethyl)-cyclohexyl]-methylamine;

(trans)C-[3,4-Dimethyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

(1S-cis)C-[3-Methyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

(1R-trans)C-[3-Methyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

(1R-cis)C-[3-Methyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

(1S-trans)C-[3-Methyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

(1α,3α,4α)C-[3,4-Dimethyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

(1α,3β,4β)C-[3,4-Dimethyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

(S)C-[3,3-Dimethyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

(R)C-[3,3-Dimethyl-1-(1H-tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

C-[3,3-Dimethyl-1-(1H-tetrazol-5-ylmethyl)-cyclobutyl]-methylamine;

N-[2-(1-Aminomethyl-cyclohexyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(1S-cis)N-[2-(1-Aminomethyl-3-methyl-cyclohexyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(trans)N-[2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(1R-cis)N-[2-(1-Aminomethyl-3-methyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(1S-trans)N-[2-(1-Aminomethyl-3-methyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(1S-cis)N-[2-(1-Aminomethyl-3-methyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(1R-trans)N-[2-(1-Aminomethyl-3-methyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(1α,3α,4α)N-[2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(1α,3β,4β)N-[2-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(S)N-[2-(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

(R)N-[2-(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

N-[2-(1-Aminomethyl-3,3-dimethyl-cyclobutyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

3-(1-Aminomethyl-cyclohexylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(1S-cis)3-(1-Aminomethyl-3-methyl-cyclohexylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(trans)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(1R-cis)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(1S-trans)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(1S-cis)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(1R-trans)3-(1-Aminomethyl-3-methyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(1α,3α,4α)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(1α,3β,4β)3-(1-Aminomethyl-3,4-dimethyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(S)3-(1-Aminomethyl-3,3-dimethyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

(R)3-(1-Aminomethyl-3,3-dimethyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

3-(1-Aminomethyl-3,3-dimethyl-cyclobutylmethyl)-4H-[1,2,4]thiadiazol-5-one;

C-[1-(2-Oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclohexyl]-methylamine;

(1S-cis)C-[3-Methyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclohexyl]-methylamine;

(trans)C-[3,4-Dimethyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(1S-cis)C-[3-Methyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(1R-trans)C-[3-Methyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(1R-cis)C-[3-Methyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(1S-trans)C-[3-Methyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(1α,3α,4α)C-[3,4-Dimethyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(1α,3β,4β)C-[3,4-Dimethyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(S)C-[3,3-Dimethyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(R)C-[3,3-Dimethyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

C-[3,3-Dimethyl-1-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclobutyl]-methylamine;

(1-Aminomethyl-cyclohexyl)-methanesulfonamide;

(1R-trans)(1-Aminomethyl-3-methyl-cyclohexyl)-methanesulfonamide;

(trans)(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-methanesulfonamide;

(1S-trans)(1-Aminomethyl-3-methyl-cyclopentyl)-methanesulfonamide;

(1R-cis)(1-Aminomethyl-3-methyl-cyclopentyl)-methanesulfonamide;

(1R-trans)(1-Aminomethyl-3-methyl-cyclopentyl)-methanesulfonamide;

(1S-cis)(1-Aminomethyl-3-methyl-cyclopentyl)-methanesulfonamide;

(1α,3β,4β)(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-methanesulfonamide;

(1α,3α,4α)(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-methanesulfonamide;

(R)(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-methanesulfonamide;

(S)(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-methanesulfonamide;

(1-Aminomethyl-3,3-dimethyl-cyclobutyl)-methanesulfonamide;

(1-Aminomethyl-cyclohexyl)-methanesulfonic acid;

(1R-trans) (1-Aminomethyl-3-methyl-cyclohexyl)-methanesulfonic acid;

(trans)(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-methanesulfonic acid;

(1S-trans)(1-Aminomethyl-3-methyl-cyclopentyl)-methanesulfonic acid;

(1S-cis)(1-Aminomethyl-3-methyl-cyclopentyl)-methanesulfonic acid;

(1R-trans)(1-Aminomethyl-3-methyl-cyclopentyl)-methanesulfonic acid;

(1R-cis)(1-Aminomethyl-3-methyl-cyclopentyl)-methanesulfonic acid;

(1α,3β,4β)(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-methanesulfonic acid;

(1α,3α,4α)(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-methanesulfonic acid;

(R)(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-methanesulfonic acid;

(S)(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-methanesulfonic acid;

(1-Aminomethyl-3,3-dimethyl-cyclobutyl)-methanesulfonic acid;

(1-Aminomethyl-cyclopentylmethyl)-phosphonic acid;

2-(1-Aminomethyl-cyclopentyl)-N-hydroxy-acetamide;

N-[2-(1-Aminomethyl-cyclopentyl)-ethyl]-methanesulfonamide;

3-(1-Aminomethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazol-5-one;

3-(1-Aminomethyl-cyclopentylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

C-[1-(1H-Tetrazol-5-ylmethyl)-cyclopentyl]-methylamine;

N-[2-(1-Aminomethyl-cyclopentyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

3-(1-Aminomethyl-cyclopentylmethyl)-4H-[1,2,4]thiadiazol-5-one;

C-[1-(2-Oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cyclopentyl]-methylamine;

(1-Aminomethyl-cyclopentyl)-methanesulfonamide;

(1-Aminomethyl-cyclopentyl)-methanesulfonic acid;

(9-Aminomethyl-bicyclo[3.3.1]non-9-ylmethyl)-phosphonic acid;

2-(9-Aminomethyl-bicyclo[3.3.1]non-9-yl)-N-hydroxy-acetamide;

N-[2-(9-Aminomethyl-bicyclo[3.3.1]non-9-yl)-ethyl]-methanesulfonamide;

3-(9-Aminomethyl-bicyclo[3.3.1]non-9-ylmethyl)-4H-[1,2,4]oxadiazol-5-one;

3-(9-Aminomethyl-bicyclo[3.3.1]non-9-ylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

C-[9-(1H-Tetrazol-5-ylmethyl)-bicyclo[3.3.1]non-9-yl]-methylamine;

N-[2-(9-Aminomethyl-bicyclo[3.3.1]non-9-yl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

3-(9-Aminomethyl-bicyclo[3.3.1]non-9-ylmethyl)-4H-[1,2,4]thiadiazol-5-one;

C-[9-(2-Oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-bicyclo[3.3.1]non-9-yl]-methylamine;

(9-Aminomethyl-bicyclo[3.3.1]non-9-yl)-methanesulfonamide;

(9-Aminomethyl-bicyclo[3.3.1]non-9-yl)-methanesulfonic acid;

(2-Aminomethyl-adamantan-2-ylmethyl)-phosphonic acid;

2-(2-Aminomethyl-adamantan-2-yl)-N-hydroxy-acetamide;

N-[2-(2-Aminomethyl-adamantan-2-yl)-ethyl]-methanesulfonamide;

3-(2-Aminomethyl-adamantan-2-ylmethyl)-4H-[1,2,4]oxadiazol-5-one;

3-(2-Aminomethyl-adamantan-2-ylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

C-[2-(1H-Tetrazol-5-ylmethyl)-adamantan-2-yl]-methylamine;

N-[2-(2-Aminomethyl-adamantan-2-yl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

3-(2-Aminomethyl-adamantan-2-ylmethyl)-4H-[1,2,4]thiadiazol-5-one;

C-[2-(2-Oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-adamantan-2-yl]-methylamine;

(2-Aminomethyl-adamantan-2-yl)-methanesulfonamide;

(2-Aminomethyl-adamantan-2-yl)-methanesulfonic acid;

(1-Aminomethyl-cycloheptylmethyl)-phosphonic acid;

2-(1-Aminomethyl-cycloheptyl)-N-hydroxy-acetamide;

N-[2-(1-Aminomethyl-cycloheptyl)-ethyl]-methanesulfonamide;

3-(1-Aminomethyl-cycloheptylmethyl)-4H-[1,2,4]oxadiazole-5-thione;

N-[2-(1-Aminomethyl-cycloheptyl)-ethyl]-C,C,C-trifluoro-methanesulfonamide;

C-[1-(2-Oxo-2,3-dihydro-2 l4-[1,2,3,5]oxathiadiazol-4-ylmethyl)-cycloheptyl]-methylamine;

(1-Aminomethyl-cycloheptyl)-methanesulfonamide;

(1-Aminomethyl-cycloheptyl)-methanesulfonic acid;

(1α,3α,4α)-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid;

(1α,3α,4α)-(1-Aminomethyl-3,4-diethyl-cyclopentyl)-acetic acid;

(1α,3α,4α)-(1-Aminomethyl-3,4-diisopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4α)]-(1-Aminomethyl-3-ethyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4α)]-(1-Aminomethyl-3-ethyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4α)]-(1-Aminomethyl-3-isopropyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4α)]-(1-Aminomethyl-3-isopropyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4α)]-(1-Aminomethyl-3-ethyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4α)]-(1-Aminomethyl-3-ethyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4α)]-(1-Aminomethyl-3-tert-butyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4α)]-(1-Aminomethyl-3-tert-butyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4α)]-(1-Aminomethyl-3-tert-butyl-4-ethyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4α)]-(1-Aminomethyl-3-tert-butyl-4-ethyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4α)]-(1-Aminomethyl-3-tert-butyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4α)]-(1-Aminomethyl-3-tert-butyl-4-isopropyl-cyclopentyl)-acetic acid;

(1α,3α,4α)-(1-Aminomethyl-3,4-di-tert-butyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4α)]-(1-Aminomethyl-3-methyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4α)]-(1-Aminomethyl-3-methyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4α)]-(1-Aminomethyl-3-benzyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4α)]-(1-Aminomethyl-3-benzyl-4-methyl-cyclopentyl)-acetic acid;

(1S-cis)-(1-Aminomethyl-3-methyl-cyclopentyl)-acetic acid;

(1S-cis)-(1-Aminomethyl-3-ethyl-cyclopentyl)-acetic acid;

(1S-cis)-(1-Aminomethyl-3-isopropyl-cyclopentyl)-acetic acid;

(1S-cis)-(1-Aminomethyl-3-tert-butyl-cyclopentyl)-acetic acid;

(1S-cis)-(1-Aminomethyl-3-phenyl-cyclopentyl)-acetic acid;

(1S-cis)-(1-Aminomethyl-3-benzyl-cyclopentyl)-acetic acid;

(1R-cis)-(1-Aminomethyl-3-methyl-cyclopentyl)-acetic acid;

(1R-cis)-(1-Aminomethyl-3-ethyl-cyclopentyl)-acetic acid;

(1R-cis)-(1-Aminomethyl-3-isopropyl-cyclopentyl)-acetic acid;

(1R-cis)-(1-Aminomethyl-3-tert-butyl-cyclopentyl)-acetic acid;

(1R-cis)-(1-Aminomethyl-3-phenyl-cyclopentyl)-acetic acid;

(1R-cis)-(1-Aminomethyl-3-benzyl-cyclopentyl)-acetic acid;

(S)-(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-acetic acid;

(S)-(1-Aminomethyl-3,3-diethyl-cyclopentyl)-acetic acid;

(1-Aminomethyl-3,3,4,4-tetramethyl-cyclopentyl)-acetic acid;

(1-Aminomethyl-3,3,4,4-tetraethyl-cyclopentyl)-acetic acid;

(1α,3β,4β)-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid;

(1α,3β,4β)-(1-Aminomethyl-3,4-diethyl-cyclopentyl)-acetic acid;

(1α,3β,4β)-(1-Aminomethyl-3,4-diisopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4β)]-(1-Aminomethyl-3-ethyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-ethyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4β)]-(1-Aminomethyl-3-isopropyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-isopropyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4β)]-(1-Aminomethyl-3-ethyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-ethyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4β)]-(1-Aminomethyl-3-tert-butyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-tert-butyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4β)]-(1-Aminomethyl-3-tert-butyl-4-ethyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-tert-butyl-4-ethyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4β)]-(1-Aminomethyl-3-tert-butyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-tert-butyl-4-isopropyl-cyclopentyl)-acetic acid;

(1α,3β,4β)-(1-Aminomethyl-3,4-di-tert-butyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4β)]-(1-Aminomethyl-3-methyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-methyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4β)]-(1-Aminomethyl-3-benzyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-benzyl-4-methyl-cyclopentyl)-acetic acid;

(1R-trans)-(1-Aminomethyl-3-methyl-cyclopentyl)-acetic acid;
(1R-trans)-(1-Aminomethyl-3-ethyl-cyclopentyl)-acetic acid;
(1R-trans)-(1-Aminomethyl-3-isopropyl-cyclopentyl)-acetic acid;
(1R-trans)-(1-Aminomethyl-3-tert-butyl-cyclopentyl)-acetic acid;
(1R-trans)-(1-Aminomethyl-3-phenyl-cyclopentyl)-acetic acid;
(1R-trans)-(1-Aminomethyl-3-benzyl-cyclopentyl)-acetic acid;
(1S-trans)-(1-Aminomethyl-3-methyl-cyclopentyl)-acetic acid;
(1S-trans)-(1-Aminomethyl-3-ethyl-cyclopentyl)-acetic acid;
(1S-trans)-(1-Aminomethyl-3-isopropyl-cyclopentyl)-acetic acid;
(1S-trans)-(1-Aminomethyl-3-tert-butyl-cyclopentyl)-acetic acid;
(1S-trans)-(1-Aminomethyl-3-phenyl-cyclopentyl)-acetic acid;
(1S-trans)-(1-Aminomethyl-3-benzyl-cyclopentyl)-acetic acid;
(R)-(1-Aminomethyl-3,3-dimethyl-cyclopentyl)-acetic acid;
(R)-(1-Aminomethyl-3,3-diethyl-cyclopentyl)-acetic acid;
cis-(1-Aminomethyl-3-methyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-ethyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-isopropyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-tert-butyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-phenyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-benzyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-methyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-ethyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-isopropyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-tert-butyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-phenyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-benzyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-ethyl-3-methyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-isopropyl-3-methyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-tert-butyl-3-methyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-methyl-3-phenyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-benzyl-3-methyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-ethyl-3-methyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-isopropyl-3-methyl-cyclobutyl)-acetic acid;

trans-(1-Aminomethyl-3-tert-butyl-3-methyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-methyl-3-phenyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-benzyl-3-methyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-ethyl-3-isopropyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-tert-butyl-3-ethyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-ethyl-3-phenyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-benzyl-3-ethyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-ethyl-3-isopropyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-tert-butyl-3-ethyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-ethyl-3-phenyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-benzyl-3-ethyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-tert-butyl-3-isopropyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-isopropyl-3-phenyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-benzyl-3-isopropyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-tert-butyl-3-phenyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-benzyl-3-tert-butyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-tert-butyl-3-isopropyl-cyclobutyl)-acetic acic
trans-(1-Aminomethyl-3-isopropyl-3-phenyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-benzyl-3-isopropyl-cyclobutyl)-acetic acid;
trans-(1-Aminomethyl-3-tert-butyl-3-phenyl-cyclobutyl)-acetic acid;
cis-(1-Aminomethyl-3-benzyl-3-tert-butyl-cyclobutyl)-acetic acid;
(1-Aminomethyl-3,3-dimethyl-cyclobutyl)-acetic acid;
(1-Aminomethyl-3,3-diethyl-cyclobutyl)-acetic acid;
(1-Aminomethyl-3,3-diisopropyl-cyclobutyl)-acetic acid;
(1-Aminomethyl-3,3-di-tert-butyl-cyclobutyl)-acetic acid;
(1-Aminomethyl-3,3-diphenyl-cyclobutyl)-acetic acid;
(1-Aminomethyl-3,3-dibenzyl-cyclobutyl)-acetic acid;
(1-Aminomethyl-2,2,4,4-tetramethyl-cyclobutyl)-acetic acid;
(1-Aminomethyl-2,2,3,3,4,4-hexamethyl-cyclobutyl)-acetic acid;
(R)-(1-Aminomethyl-2,2-dimethyl-cyclobutyl)-acetic acid;
(S)-(1-Aminomethyl-2,2-dimethyl-cyclobutyl)-acetic acid;
(1R-cis)-(1-Aminomethyl-2-methyl-cyclobutyl)-acetic acid;

[1R-(1α,2α,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclobutyl)-acetic acid;

(1α,2α,4α)-(1-Aminomethyl-2,4-dimethyl-cyclobutyl)-acetic acid;

[1R-(1α,2α,3β)]-(1-Aminomethyl-2,3-dimethyl-cyclobutyl)-acetic acid;

(1α,2α,4β)-(1-Aminomethyl-2,4-dimethyl-cyclobutyl)-acetic acid;

(1S-trans)-(1-Aminomethyl-2-methyl-cyclobutyl)-acetic acid;

[1S-(1α,2β,3β)]-(1-Aminomethyl-2,3-dimethyl-cyclobutyl)-acetic acid;

(1α,2β,4β)- (1-Aminomethyl-2,4-dimethyl-cyclobutyl)-acetic acid;

[1S-(1α,2β,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclobutyl)-acetic acid;

(1α,2β,4α)-(1-Aminomethyl-2,4-dimethyl-cyclobutyl)-acetic acid;

(1R-trans)-(1-Aminomethyl-2-methyl-cyclobutyl)-acetic acid;

[1R-(1α,2β,3β)]-(1-Aminomethyl-2,3-dimethyl-cyclobutyl)-acetic acid;

[1R-(1α,2β,4β)]-(1-Aminomethyl-2-ethyl-4-methyl-cyclobutyl)-acetic acid;

[1R-(1α,2β,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclobutyl)-acetic acid;

(1α,2β,4α)-(1-Aminomethyl-2,4-dimethyl-cyclobutyl)-acetic acid;

(1S-cis)-(1-Aminomethyl-2-methyl-cyclobutyl)-acetic acid;

[1S-(1α,2α,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclobutyl)-acetic acid;

[1S-(1α,2α,3α)]-(1-Aminomethyl-2,4-dimethyl-cyclobutyl)-acetic acid;

[1S-(1α,2β,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclobutyl)-acetic acid;

(1α,2α,4β)-(1-Aminomethyl-2,4-dimethyl-cyclobutyl)-acetic acid;

(3S, 4S)-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid;

(3R, 4R)-(1-Aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid;

(3S, 4S))-(1-Aminomethyl-3,4-diethyl-cyclopentyl)-acetic acid;

(3R, 4R)-(1-Aminomethyl-3,4-diethyl-cyclopentyl)-acetic acid;

(3S, 4S)-(1-Aminomethyl-3,4-diisopropyl-cyclopentyl)-acetic acid;

(3R, 4R)-(1-Aminomethyl-3,4-diisopropyl-cyclopentyl)-acetic acid;

(3S, 4S)-(1-Aminomethyl-3,4-di-tert-butyl-cyclopentyl)-acetic acid;

(3R, 4R)-(1-Aminomethyl-3,4-di-tert-butyl-cyclopentyl)-acetic acid;

(3S, 4S)-(1-Aminomethyl-3,4-diphenyl-cyclopentyl)-acetic acid;

(3R, 4R)-(1-Aminomethyl-3,4-diphenyl-cyclopentyl)-acetic acid;

(3S, 4S)-(1-Aminomethyl-3,4-dibenzyl-cyclopentyl)-acetic acid;

(3R, 4R)-(1-Aminomethyl-3,4-dibenzyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-methyl-4-ethyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-methyl-4-ethyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-methyl-4-ethyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-methyl-4-ethyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-methyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-methyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-methyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-methyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-methyl-4-tert-butyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-methyl-4-tert-butyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-methyl-4-tert-butyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4β)]-(1-Aminomethyl-3-methyl-4-tert-butyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-methyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-methyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-methyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-methyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-methyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-methyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-ethyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-ethyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-ethyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-ethyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-tert-butyl-4-ethyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-tert-butyl-4-ethyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-tert-butyl-4-ethyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-tert-butyl-4-ethyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-ethyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-ethyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-ethyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-ethyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-ethyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-ethyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-ethyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-ethyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-tert-butyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-tert-butyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-tert-butyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-tert-butyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-isopropyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-isopropyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-isopropyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-isopropyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-isopropyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-isopropyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-tert-butyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-tert-butyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-tert-butyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-tert-butyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-tert-butyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-tert-butyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-tert-butyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-tert-butyl-cyclopentyl)-acetic acid;

[1S-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-phenyl-cyclopentyl)-acetic acid;

[1R-(1α,3α,4β)]-(1-Aminomethyl-3-benzyl-4-phenyl-cyclopentyl)-acetic acid;

[1S-(1α,3β,4α)]-(1-Aminomethyl-3-benzyl-4-phenyl-cyclopentyl)-acetic acid;

(1R-cis)-(1-Aminomethyl-2-methyl-cyclopentyl)-acetic acid;

(1S-cis)-(1-Aminomethyl-2-methyl-cyclopentyl)-acetic acid;

(1R-trans)-(1-Aminomethyl-2-methyl-cyclopentyl)-acetic acid;
(1S-trans)-(1-Aminomethyl-2-methyl-cyclopentyl)-acetic acid;
(R)-(1-Aminomethyl-2,2-dimethyl-cyclopentyl)-acetic acid;
(S)-(1-Aminomethyl-2,2-dimethyl-cyclopentyl)-acetic acid;
(1-Aminomethyl-2,2,5,5-tetramethyl-cyclopentyl)-acetic acid;
(1α,2β,5β)-(1-Aminomethyl-2,5-dimethyl-cyclopentyl)-acetic acid;
(2R, 5R)-(1-Aminomethyl-2,5-dimethyl-cyclopentyl)-acetic acid;
(2S. 5S)-(1-Aminomethyl-2,5-dimethyl-cyclopentyl)-acetic acid;
(1α,2α,5α)-(1-Aminomethyl-2,5-dimethyl-cyclopentyl)-acetic acid;
[1R-(1α,2α,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclopentyl)-acetic acid;
[1R-(1α,2β,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclopentyl)-acetic acid;
[1R-(1α,2α,3β)]-(1-Aminomethyl-2,3-dimethyl-cyclopentyl)-acetic acid;
[1R-(1α,2β,3β)]-(1-Aminomethyl-2,3-dimethyl-cyclopentyl)-acetic acid;
[1S-(1α,2α,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclopentyl)-acetic acid;
[1S-(1α,2β,3α)]-(1-Aminomethyl-2,3-dimethyl-cyclopentyl)-acetic acid;
[1S-(1α,2α,3β)]-(1-Aminomethyl-2,3-dimethyl-cyclopentyl)-acetic acid;
[1S-(1α,2β,3β)]-(1-Aminomethyl-2,3-dimethyl-cyclopentyl)-acetic acid;
[1R-(1α,2α,4α)]-(1-Aminomethyl-2,4-dimethyl-cyclopentyl)-acetic acid;
[1S-(1α,2α,4α)]-(1-Aminomethyl-2,4-dimethyl-cyclopentyl)-acetic acid;
[1R-(1α,2α,4β)]-(1-Aminomethyl-2,4-dimethyl-cyclopentyl)-acetic acid;
[1S-(1α,2α,4β)]-(1-Aminomethyl-2,4-dimethyl-cyclopentyl)-acetic acid;
[1R-(1α,2β,4α)]-(1-Aminomethyl-2,4-dimethyl-cyclopentyl)-acetic acid;
[1S-(1α,2β,4α)]-(1-Aminomethyl-2,4-dimethyl-cyclopentyl)-acetic acid;
[1R-(1α,2β,4β)]-(1-Aminomethyl-2,4-dimethyl-cyclopentyl)-acetic acid;

and

[1S-(1α,2β,4β)]-(1-Aminomethyl-2,4-dimethyl-cyclopentyl)-acetic acid.

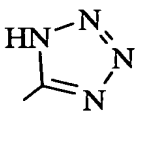
Other preferred embodiments of the invention methods utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH, wherein R is a sulfonamide selected from $-NHSO_2R^{15}$ or $-SO_2NHR^{15}$ wherein R^{15} is straight or branched alkyl or trifluoromethyl.

Other preferred embodiments of the invention methods utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH that is N-[2-(1-aminomethyl-cyclohexyl)-ethyl]-methanesulfonamide.

Other preferred embodiments of the invention methods utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH, wherein R is a phosphonic acid, $-PO_3H_2$.

Other preferred embodiment of the invention methods utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH that is (1-aminomethyl-cyclohexylmethyl)-phosphonic acid and (2-aminomethyl-4-methyl-pentyl)-phosphonic acid.

Other preferred embodiments of the invention methods utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH, wherein other preferred compounds are those wherein R is a heterocycle selected from: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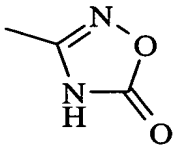
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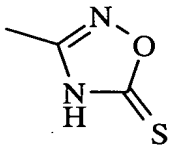
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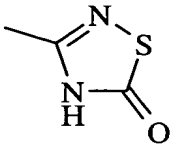
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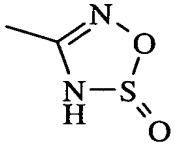
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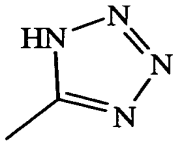
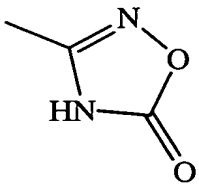
Other preferred embodiments of the invention methods are those that utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH, that is C-[1-(1H-tetrazol-5-ylmethyl)cyclohexyl]-methylamine or 4-methyl-2-(1H-tetrazol-5-ylmethyl)-pentylamine.

Especially preferred embodiments of the invention methods utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH wherein:

m is an integer of from 0 to 2;

p is an integer of 2; and

R is  or 
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Other more preferred embodiments of the invention methods are those that utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH that is 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one, or a pharmaceutically acceptable salt thereof.

Other more preferred embodiments of the invention methods are those that utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH that is 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride.

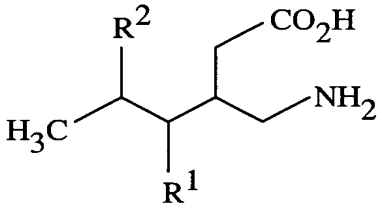
Other more preferred embodiments of the invention methods are those that utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH that is 3-(1-aminomethyl-cycloheptylmethyl)-4H-[1,2,4]oxadiazol-5-one, or a pharmaceutically acceptable salt thereof.

Other more preferred embodiments of the invention methods are those that utilize a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH that is 3-(1-aminomethyl-cycloheptylmethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride.

Other more preferred embodiments of the invention methods are those that utilizes a compound of the Formula III, IIIC, IIIF, IIIG, or IIIH that is C-[1-(1H-tetrazol-5-ylmethyl)-cycloheptyl]-methylamine, or a pharmaceutically acceptable salt thereof.

Alpha2delta ligands of the Formulas III, IIIC, IIIF, IIIG, and IIIH, and methods of synthesizing them, are described in PCT Patent Application No. WO 99/31075, which is incorporated herein by reference in its entirety.

Other preferred embodiments of the invention methods utilize an alpha2delta ligand that is a compound of the Formula IV



IV

or a pharmaceutically acceptable salt thereof wherein:

R^1 is hydrogen, straight or branched alkyl of from 1 to 6 carbon atoms or phenyl;

R^2 is straight or branched alkyl of from 1 to 8 carbon atoms,
straight or branched alkenyl of from 2 to 8 carbon atoms,
cycloalkyl of from 3 to 7 carbon atoms,
alkoxy of from 1 to 6 carbon atoms,

-alkylcycloalkyl,

-alkylalkoxy,

-alkyl OH

-alkylphenyl,

-alkylphenoxy,

-phenyl or substituted phenyl; and

R^1 is straight or branched alkyl of from 1 to 6 carbon atoms or phenyl when R^2 is methyl.

Other preferred embodiments of the invention methods are those that employ a compound of Formula IV wherein R^1 is hydrogen, and R^2 is alkyl.

Other preferred embodiments of the invention methods are those that that employ a compound of Formula IV wherein R^1 is methyl, and R^2 is alkyl.

Other preferred embodiments of the invention methods are those that employ a compound of Formula IV wherein R^1 is methyl, and R^2 is methyl or ethyl.

Other preferred embodiments of the invention methods are those that employ a compound of Formula IV selected from:

3-Aminomethyl-5-methylheptanoic acid;

3-Aminomethyl-5-methyl-octanoic acid;

3-Aminomethyl-5-methyl-nonanoic acid;

3-Aminomethyl-5-methyl-decanoic acid;

3-Aminomethyl-5-methyl-undecanoic acid;

3-Aminomethyl-5-methyl-dodecanoic acid;

3-Aminomethyl-5-methyl-tridecanoic acid;

3-Aminomethyl-5-cyclopropyl-hexanoic acid;

3-Aminomethyl-5-cyclobutyl-hexanoic acid;

3-Aminomethyl-5-cyclopentyl-hexanoic acid;

3-Aminomethyl-5-cyclohexyl-hexanoic acid;

3-Aminomethyl-5-trifluoromethyl-hexanoic acid;

3-Aminomethyl-5-phenyl-hexanoic acid;

3-Aminomethyl-5-(2-chlorophenyl)-hexanoic acid;
3-Aminomethyl-5-(3-chlorophenyl)-hexanoic acid;
3-Aminomethyl-5-(4-chlorophenyl)-hexanoic acid;
3-Aminomethyl-5-(2-methoxyphenyl)-hexanoic acid;
3-Aminomethyl-5-(3-methoxyphenyl)-hexanoic acid;
3-Aminomethyl-5-(4-methoxyphenyl)-hexanoic acid; and
3-Aminomethyl-5-(phenylmethyl)-hexanoic acid.
(3R,4S)-3-Aminomethyl-4,5-dimethyl-hexanoic acid;
3-Aminomethyl-4,5-dimethyl-hexanoic acid;
(3R,4S)-3-Aminomethyl-4,5-dimethyl-hexanoic acid MP;
(3S,4S)-3-Aminomethyl-4,5-dimethyl-hexanoic acid;
(3R,4R)-3-Aminomethyl-4,5-dimethyl-hexanoic acid MP;
3-Aminomethyl-4-isopropyl-hexanoic acid;
3-Aminomethyl-4-isopropyl-heptanoic acid;
3-Aminomethyl-4-isopropyl-octanoic acid;
3-Aminomethyl-4-isopropyl-nonanoic acid;
3-Aminomethyl-4-isopropyl-decanoic acid;
3-Aminomethyl-4-phenyl-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-methoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-ethoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-propoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-isopropoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-*tert*-butoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-fluoromethoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(2-fluoro-ethoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(3,3,3-trifluoro-propoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-phenoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(4-chloro-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(3-chloro-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(2-chloro-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(4-fluoro-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(3-fluoro-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(2-fluoro-phenoxy)-hexanoic acid;

(3S,5S)-3-Aminomethyl-5-(4-methoxy-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(3-methoxy-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(2-methoxy-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(4-nitro-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(3-nitro-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-(2-nitro-phenoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-hydroxy-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-methoxy-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-ethoxy-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-methyl-6-propoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-isopropoxy-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-*tert*-butoxy-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-fluoromethoxy-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(2-fluoro-ethoxy)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-methyl-6-(3,3,3-trifluoro-propoxy)-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-methyl-6-phenoxy-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(4-chloro-phenoxy)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(3-chloro-phenoxy)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(2-chloro-phenoxy)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(4-fluoro-phenoxy)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(3-fluoro-phenoxy)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(2-fluoro-phenoxy)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(4-methoxy-phenoxy)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(3-methoxy-phenoxy)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(2-methoxy-phenoxy)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl 6-(4-trifluoromethyl-phenoxy)-hexanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl 6-(3-trifluoromethyl-phenoxy)-hexanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl 6-(2-trifluoromethyl-phenoxy)-hexanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl 6-(4-nitro-phenoxy)-hexanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl 6-(3-nitro-phenoxy)-hexanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl 6-(2-nitro-phenoxy)-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-benzyloxy-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-7-hydroxy-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-methoxy-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-ethoxy-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-propoxy-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-isopropoxy-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-*tert*-butoxy-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-fluoromethoxy-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(2-fluoro-ethoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-(3,3,3-trifluoro-propoxy)-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-benzyloxy-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-phenoxy-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(4-chloro-phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(3-chloro-phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(2-chloro-phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(4-fluoro-phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(3-fluoro-phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(2-fluoro-phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(4-methoxy-phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(3- methoxy -phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-7-(2- methoxy -phenoxy)-5-methyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-(4-trifluoromethyl-phenoxy)-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-(3-trifluoromethyl-phenoxy)-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-(2-trifluoromethyl-phenoxy)-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-(4-nitro-phenoxy)-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-(3-nitro-phenoxy)-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-7-(2-nitro-phenoxy)-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-6-phenyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(4-chloro-phenyl)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(3-chloro-phenyl)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(2-chloro-phenyl)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(4-methoxy-phenyl)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(3-methoxy-phenyl)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(2-methoxy-phenyl)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(4-fluoro-phenyl)-5-methyl-hexanoic acid;

(3S,5S)-3-Aminomethyl-6-(3-fluoro-phenyl)-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-6-(2-fluoro-phenyl)-5-methyl-hexanoic acid;
(3S,5R)-3-Aminomethyl-5-methyl-7-phenyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(4-chloro-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(3-chloro-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(2-chloro-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(4-methoxy-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(3-methoxy-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(2-methoxy-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(4-fluoro-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(3-fluoro-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-(2-fluoro-phenyl)-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-5-methyl-oct-7-enoic acid;
(3S,5R)-3-Aminomethyl-5-methyl-non-8-enoic acid;
(E)-(3S,5S)-3-Aminomethyl-5-methyl-oct-6-enoic acid;
(Z)-(3S,5S)-3-Aminomethyl-5-methyl-oct-6-enoic acid;
(Z)-(3S,5S)-3-Aminomethyl-5-methyl-non-6-enoic acid;
(E)-(3S,5S)-3-Aminomethyl-5-methyl-non-6-enoic acid;
(E)-(3S,5R)-3-Aminomethyl-5-methyl-non-7-enoic acid;
(Z)-(3S,5R)-3-Aminomethyl-5-methyl-non-7-enoic acid;
(Z)-(3S,5R)-3-Aminomethyl-5-methyl-dec-7-enoic acid;
(E)-(3S,5R)-3-Aminomethyl-5-methyl-undec-7-enoic acid;
(3S,5S)-3-Aminomethyl-5,6, 6-trimethyl-heptanoic acid;
(3S,5S)-3-Aminomethyl-5,6-dimethyl-heptanoic acid;

(3S,5S)-3-Aminomethyl-5-cyclopropyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-cyclobutyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-cyclopentyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-5-cyclohexyl-hexanoic acid;

(3S,5R)-3-Aminomethyl-5-methyl-heptanoic acid;

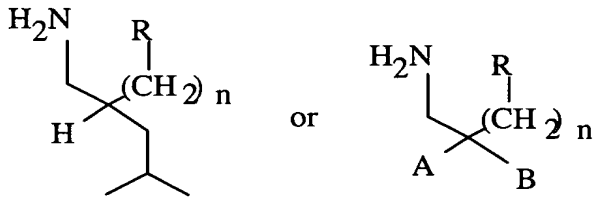
(3S,5R)-3-Aminomethyl-5-methyl-octanoic acid;
(3S,5R)-3-Aminomethyl-5-methyl-nonanoic acid;
(3S,5R)-3-Aminomethyl-5-methyl-decanoic acid;
(3S,5R)-3-Aminomethyl-5-methyl-undecanoic acid;
(3S,5R)-3-Aminomethyl-5-methyl-dodecanoic acid;
(3S,5R)-3-Aminomethyl-5,9-dimethyl-decanoic acid;
(3S,5R)-3-Aminomethyl-5,7-dimethyl-octanoic acid;
(3S,5R)-3-Aminomethyl-5,8-dimethyl-nonanoic acid;
(3S,5R)-3-Aminomethyl-6-cyclopropyl-5-methyl-hexanoic acid;
(3S,5R)-3-Aminomethyl-6-cyclobutyl-5-methyl-hexanoic acid;
(3S,5R)-3-Aminomethyl-6-cyclopentyl-5-methyl-hexanoic acid;
(3S,5R)-3-Aminomethyl-6-cyclohexyl-5-methyl-hexanoic acid;
(3S,5R)-3-Aminomethyl-7-cyclopropyl-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-cyclobutyl-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-cyclopentyl-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-7-cyclohexyl-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-8-cyclopropyl-5-methyl-octanoic acid;
(3S,5R)-3-Aminomethyl-8-cyclobutyl-5-methyl-octanoic acid;
(3S,5R)-3-Aminomethyl-8-cyclopentyl-5-methyl-octanoic acid;
(3S,5R)-3-Aminomethyl-8-cyclohexyl-5-methyl-octanoic acid;
(3S,5S)-3-Aminomethyl-6-fluoro-5-methyl-hexanoic acid;
(3S,5S)-3-Aminomethyl-7-fluoro-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-8-fluoro-5-methyl-octanoic acid;
(3S,5R)-3-Aminomethyl-9-fluoro-5-methyl-nonanoic acid;
(3S,5S)-3-Aminomethyl-7,7,7-trifluoro-5-methyl-heptanoic acid;
(3S,5R)-3-Aminomethyl-8,8,8-trifluoro-5-methyl-octanoic acid;
(3S,5R)-3-Aminomethyl-5-methyl-8-phenyl-octanoic acid;

(3S,5S)-3-Aminomethyl-5-methyl-6-phenyl-hexanoic acid; and

(3S,5R)-3-Aminomethyl-5-methyl-7-phenyl-heptanoic acid.

Alpha2delta ligands of the Formula IV, and methods of synthesizing them are described in PCT Patent Application No. WO 00/76958, which is incorporated herein by reference in its entirety.

Other preferred embodiments of the invention methods utilize an alpha2delta ligand which is a compound of the Formula (IXA) or (IXB)



(IXA) (IXB)

or a pharmaceutically acceptable salt thereof, wherein:

n is an integer of from 0 to 2;

R is sulfonamide,

amide,

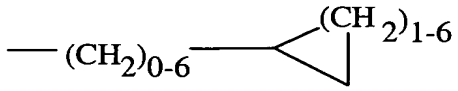
phosphonic acid,

heterocycle,

sulfonic acid, or

hydroxamic acid;

A is hydrogen or methyl; and

B is 

a straight or branched alkyl of from 1 to 11 carbons, or

$-(CH_2)_{1-4}-Y-(CH_2)_{0-4}$-phenyl wherein Y is -O-, -S-, $-NR'_3$ wherein:

R'_3 is alkyl of from 1 to 6 carbons, cycloalkyl of from 3 to 8 carbons, benzyl or phenyl wherein benzyl or phenyl can be unsubstituted or substituted with from 1 to 3 substituents each independently

selected from alkyl, alkoxy, halogen, hydroxy, carboxy, carboalkoxy, trifluoromethyl, and nitro.

Other preferred embodiments of the invention methods utilize an alpha2delta ligand that is a compound of the Formula (IXA) or (IXB), wherein R is a sulfonamide selected from $-NHSO_2R^{15}$ and $-SO_2NHR^{15}$, wherein R^{15} is straight or branched alkyl or trifluoromethyl.

Other preferred embodiments of the invention methods utilize a compound of the Formula (IXA) or (IXB) selected from:

4-Methyl-2-(1H-tetrazol-5-ylmethyl)-pentylamine;

3-(2-Aminomethyl-4-methyl-pentyl)-4H-[1,2,4]oxadiazole-5-thione, HCl;

(2-Aminomethyl-4-methyl-pentyl)-phosphonic acid;

3-(3-Amino-2-cyclopentyl-propyl)-4H-[1,2,4]oxadiazol-5-one;

3-(3-Amino-2-cyclopentyl-propyl)-4H-[1,2,4]thiadiazol-5-one;

2-Cyclopentyl-3-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-yl)-propylamine;

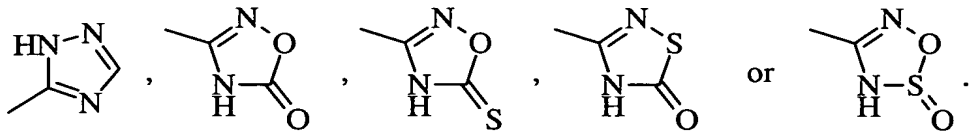
3-(3-Amino-2-cyclobutyl-propyl)-4H-[1,2,4]oxadiazol-5-one;

3-(3-Amino-2-cyclobutyl-propyl)-4H-[1,2,4]thiadiazol-5-one; and

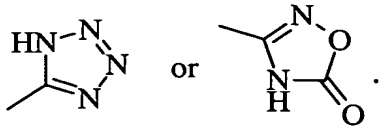
2-Cyclobutyl-3-(2-oxo-2,3-dihydro-2λ^4-[1,2,3,5]oxathiadiazol-4-yl)-propylamine.

Other preferred embodiments of the invention methods utilize a compound of the Formula (IXA) or (IXB), wherein R is a phosphonic acid, $-PO_3H_2$.

Other preferred embodiments of the invention methods utilize a compound of the Formula (IXA) or (IXB), wherein R is



Other preferred embodiments of the invention methods utilize a compound of the Formula (IXA) or (IXB) wherein R is

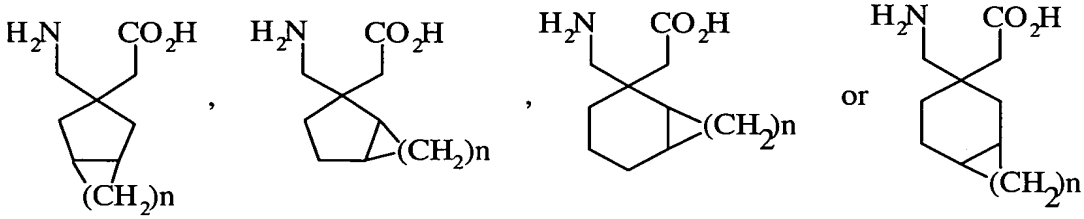


Other preferred embodiments of the invention methods utilize a compound of the Formula (IXA) or (IXB) that is 3-(2-aminomethyl-4-methyl-pentyl)-4H-[1,3,4]oxadiazol-5-one, or a pharmaceutically acceptable salt thereof.

Other preferred embodiments of the invention methods utilize a compound of the Formula (IXA) or (IXB) that is 3-(2-aminomethyl-4-methyl-pentyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride.

Alpha2delta ligands of the Formulas (IXA) and (IXB), and methods of synthesizing them, are described in PCT Patent Application No. WO 99/31074. This application is incorporated herein by reference in its entirety.

Other preferred embodiments of the invention methods utilize an alpha2delta ligand that is a compound of the Formula V, VI, VII, or VIII



V VI VII VIII

or a pharmaceutically acceptable salt thereof, wherein n is integer of from 1 to 4, where there are stereocenters, each center may be independently R or S.

Other preferred embodiments of the invention methods utilize a compound of the Formula V, VI, VII, or VIII, or a pharmaceutically acceptable salt thereof, wherein n is an integer of from 2 to 4.

Other preferred embodiments of the invention methods utilize a compound of the Formula V or a pharmaceutically acceptable salt thereof.

Other preferred embodiments of the invention methods utilize a compound of the Formula V, VI, VII, or VIII, or a pharmaceutically

acceptable salt thereof, that is selected from the following compounds and their pharmaceutically acceptable salts:

(1α,6α,8β)(2-Aminomethyl-octahydro-inden-2-yl)-acetic acid;
(2-Aminomethyl-octahydro-inden-2-yl)-acetic acid;
(2-Aminomethyl-octahydro-pentalen-2-yl)-acetic acid;
(2-Aminomethyl-octahydro-pentalen-2-yl)-acetic acid;
(3-Aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid;
(3-Aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid;
(2-Aminomethyl-octahydro-inden-2-yl)-acetic acid;
(1α,5β)(3-Aminomethyl-bicyclo[3.1.0]hex-3-yl)-acetic acid,
(1α,5β)(3-Aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid,
(1α,5β)(2-Aminomethyl-octahydro-pentalen-2-yl)-acetic acid,
(1α,6β)(2-Aminomethyl-octahydro-inden-2-yl)-acetic acid,
(1α,7β)(2-Aminomethyl-decahydro-azulen-2-yl)-acetic acid,
(1α,5β)(3-Aminomethyl-bicyclo[3.1.0]hex-3-yl)-acetic acid,
(1α,5β)(3-Aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid,
(1α,5β)(2-Aminomethyl-octahydro-pentalen-2-yl)-acetic acid,
(1α,6β)(2-Aminomethyl-octahydro-inden-2-yl)-acetic acid,
(1α,7β)(2-Aminomethyl-decahydro-azulen-2-yl)-acetic acid,
(1α,3α,5α)(3-Aminomethyl-bicyclo[3.1.0]hex-3-yl)-acetic acid,
(1α,3α,5α)(2-Aminomethyl-octahydro-pentalen-2-yl)-acetic acid,
(1α,6α,8α)(2-Aminomethyl-octahydro-inden-2-yl)-acetic acid,
(1α,7α,9α)(2-Aminomethyl-decahydro-azulen-2-yl)-acetic acid,
(1α,3β,5α)(3-Aminomethyl-bicyclo[3.1.0]hex-3-yl)-acetic acid,
(1α,3β,5α)(3-Aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid,
(1α,3β,5α)(2-Aminomethyl-octahydro-pentalen-2-yl)-acetic acid,
(1α,6α,8β)(2-Aminomethyl-octahydro-inden-2-yl)-acetic acid,
(1α,7α,9β)(2-Aminomethyl-decahydro-azulen-2-yl)-acetic acid,
((1R,3R,6R)-3-Aminomethyl-bicyclo[4.1.0]hept-3-yl)-acetic acid,
((1R,3S,6R)-3-Aminomethyl-bicyclo[4.1.0]hept-3-yl)-acetic acid,
((1S,3S,6S)-3-Aminomethyl-bicyclo[4.1.0]hept-3-yl)-acetic acid,
((1S,3R,6S)-3-Aminomethyl-bicyclo[4.1.0]hept-3-yl)-acetic acid,

((1R,3R,6S)-3-Aminomethyl-bicyclo[4.2.0]oct-3-yl)-acetic acid,
((1R,3S,6S)-3-Aminomethyl-bicyclo[4.2.0]oct-3-yl)-acetic acid,
((1S,3S,6R)-3-Aminomethyl-bicyclo[4.2.0]oct-3-yl)-acetic acid,
((1S,3R,6R)-3-Aminomethyl-bicyclo[4.2.0]oct-3-yl)-acetic acid,
((3αR,5R,7αS)-5-Aminomethyl-octahydro-inden-5-yl)-acetic acid,
((3αR,5S,7αS)-5-Aminomethyl-octahydro-inden-5-yl)-acetic acid,
((3αS,5S,7αR)-5-Aminomethyl-octahydro-inden-5-yl)-acetic acid,
((3αS,5R,7αR)-5-Aminomethyl-octahydro-inden-5-yl)-acetic acid,
((2R,4αS,8αR)-2-Aminomethyl-decahydro-naphthalen-2-yl)-acetic acid,
((2S,4αS,8αR)-2-Aminomethyl-decahydro-naphthalen-2-yl)-acetic acid,
((2S,4αR,8αS)-2-Aminomethyl-decahydro-naphthalen-2-yl)-acetic acid,
((2R,4αR,8αS)-2-Aminomethyl-decahydro-naphthalen-2-yl)-acetic acid,
((2R,4αS,9αR)-2-Aminomethyl-decahydro-benzocyclophepten-2-yl)-acetic acid,
((2S,4αS,9αR)-2-Aminomethyl-decahydro-benzocyclophepten-2-yl)-acetic acid,
((2S,4αR,9αS)-2-Aminomethyl-decahydro-benzocyclophepten-2-yl)-acetic acid,
((2R,4αR,9αS)-2-Aminomethyl-decahydro-benzocyclophepten-2-yl)-acetic acid,
((1R,3R,6S)-3-Aminomethyl-bicyclo[4.1.0]hept-3-yl)-acetic acid,
((1R,3S,6S)-3-Aminomethyl-bicyclo[4.1.0]hept-3-yl)-acetic acid,
((1S,3S,6R)-3-Aminomethyl-bicyclo[4.1.0]hept-3-yl)-acetic acid,
((1S,3R,6R)-3-Aminomethyl-bicyclo[4.1.0]hept-3-yl)-acetic acid,
((1R,3R,6R)-3-Aminomethyl-bicyclo[4.2.0]oct-3-yl)-acetic acid,
((1R,3S,6R)-3-Aminomethyl-bicyclo[4.2.0]oct-3-yl)-acetic acid,
((1S,3S,6S)-3-Aminomethyl-bicyclo[4.2.0]oct-3-yl)-acetic acid,
((1S,3R,6S)-3-Aminomethyl-bicyclo[4.2.0]oct-3-yl)-acetic acid,

((3αR,5R,7αR)-5-Aminomethyl-octahydro-inden-5-yl)-acetic acid,

((3αR,5S,7αR)-5-Aminomethyl-octahydro-inden-5-yl)-acetic acid,

((3αS,5S,7αS)-5-Aminomethyl-octahydro-inden-5-yl)-acetic acid,

((3αS,5R,7αS)-5-Aminomethyl-octahydro-inden-5-yl)-acetic acid,

((2R,4αR,8αR)-2-Aminomethyl-decahydro-naphthalen-2-yl)-acetic acid,

((2S,4αS,8αR)-2-Aminomethyl-decahydro-naphthalen-2-yl)-acetic acid,

((2S,4αR,8αS)-2-Aminomethyl-decahydro-naphthalen-2-yl)-acetic acid,

((2R,4αS,8αS)-2-Aminomethyl-decahydro-naphthalen-2-yl)-acetic acid,

((2R,4αR,9αR)-2-Aminomethyl-decahydro-benzocyclophepten-2-yl)-acetic acid,

((2S,4αR,9αR)-2-Aminomethyl-decahydro-benzocyclophepten-2-yl)-acetic acid,

((2S,4αS,9αS)-2-Aminomethyl-decahydro-benzocyclophepten-2-yl)-acetic acid, and

((2R,4αS,9αS)-2-Aminomethyl-decahydro-benzocyclophepten-2-yl)-acetic acid.

Other preferred embodiments of the invention methods utilize an alpha2delta ligand of the Formula V, VI, VII, or VIII that is (1α,3α,5α)(3-aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid, or a pharmaceutically acceptable salt thereof.

Other preferred embodiments of the invention methods utilize an alpha2delta ligand of the Formula V, VI, VII, or VIII that is (1α,3α,5α)(3-aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid hydrochloride.

PCT Patent Application No. WO 01/28978, which is incorporated herein by reference in its entirety, describes alpha2delta ligands that are compounds of the Formulas V, VI, VII, and VIII, and methods of synthesizing them.

Other preferred embodiments of the invention methods utilize an alpha2delta ligand that is selected from the following compounds and their pharmaceutically acceptable salts:

3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one;

(S,S)-(1-aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid;

(R,S)-3-aminomethyl-5-methyl-octanoic acid;

(S,R)-3-aminomethyl-5-methyl-octanoic acid;

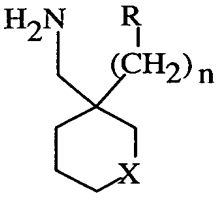
(3-aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid;

(3-aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid, wherein the cyclobutyl ring is trans to the methylamine group; and

C-[1-(1H-tetrazol-5-ylmethyl)-cycloheptyl]-methylamine.

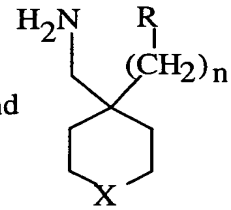
These compounds can be prepared as described below or in PCT Patent Application WO 99/21824, published May 6, 1999, PCT Patent Application WO 00/76958, published December 21, 2000, or PCT Patent Application WO 01/28978, published April 26, 2001. These applications are incorporated herein by reference in their entireties.

Other alpha2delta ligands that can be used in preferred embodiments of the invention methods are described in PCT Patent Application No. WO 99/31057, which is incorporated herein by reference in its entirety. Such alpha2delta ligands are compounds of the Formulas (XII) and (XIII)



(XII)

and



(XIII)

or a pharmaceutically acceptable salt thereof wherein:

n is an integer of from 0 to 2;

R is sulfonamide,

amide,

phosphonic acid,

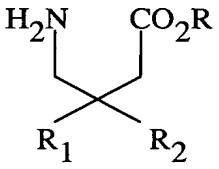
heterocycle,

sulfonic acid, or

hydroxamic acid; and

X is -O-, -S-, -S(O)-, $-S(O)_2-$,or NR'_1 wherein R'_1 is hydrogen, straight or branched alkyl of from 1 to 6 carbons, benzyl, $-C(O)R'_2$ wherein R'_2 is straight or branched alkyl of 1 to 6 carbons, benzyl or phenyl or $-CO_2R'_3$ wherein R'_3 is straight or branched alkyl of from 1 to 6 carbons, or benzyl wherein the benzyl or phenyl groups can be unsubstituted or substituted by from 1 to 3 substituents selected from halogen, trifluoromethyl, and nitro.

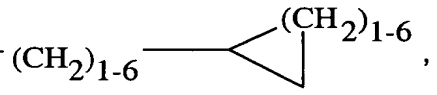
Other alpha2delta ligands that may be utilized in preferred embodiments of the invention methods are described, along with mehods of synthesizing them, in PCT Patent Application No. WO 98/17627, which is incorporated herein by reference in its entirety. Such alpha2delta ligands are compounds of the formula



or a pharmaceutically acceptable salt thereof wherein:

R is hydrogen or lower alkyl;

R_1 is hydrogen or lower alkyl;

R_2 is  ,

a straight or branched alkyl of from 7 to 11 carbon atoms, or

$-(CH_2)_{(1-4)}-X-(CH_2)_{(0-4)}$-phenyl wherein

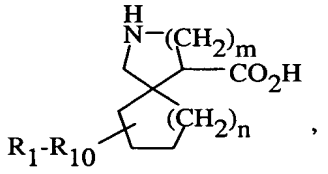
X is -O-, -S-, $-NR_3-$ wherein

R_3 is alkyl of from 1 to 6 carbons, cycloalkyl of from 3 to 8 carbons, benzyl or phenyl;

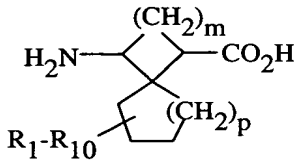
wherein phenyl and benzyl can be unsubstituted or substituted with from 1 to 3 substituents each independently selected from

alkyl, alkoxy, halogen, hydroxy, carboxy, carboalkoxy, trifluoromethyl, amino, and nitro.

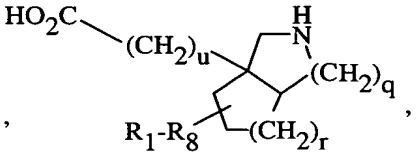
Other alpha2delta ligands that can be utilized in preferred embodiments of the invention methods are described, along with methods of synthesizing them, in PCT Patent Application No. WO 99/61424, which is incorporated herein by reference in its entirety. Such alpha2delta ligands are compounds of the formulas (1), (2), (3), (4), (5), (6), (7), and (8)



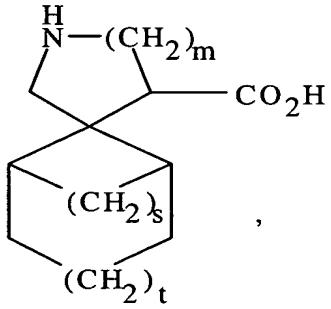
(1)



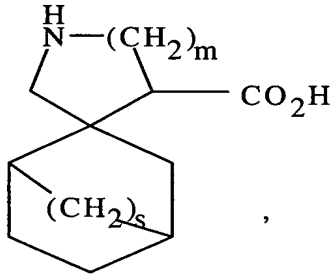
(2)



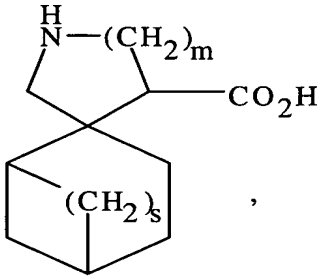
(3)



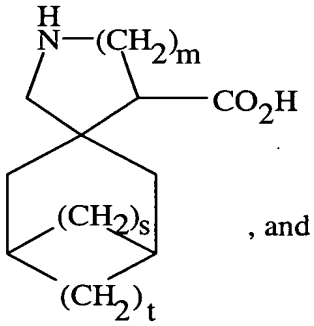
(4)



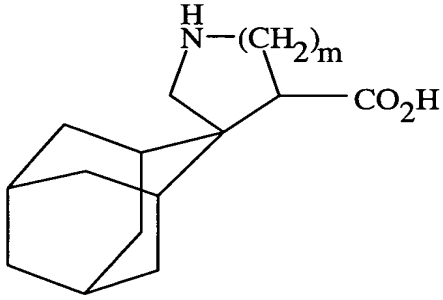
(5)



(6)



(7)



(8)

and the pharmaceutically acceptable salts and prodrugs of such compounds wherein:

R_1 to R_{10} are each independently selected from hydrogen or a straight or branched alkyl of from 1 to 6 carbons, benzyl, or phenyl;

m is an integer of from 0 to 3;

n is an integer of from 1 to 2;

o is an integer of from 0 to 3;

p is an integer of from 1 to 2;

q is an integer of from 0 to 2;

r is an integer of from 1 to 2;

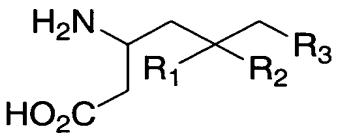
s is an integer of from 1 to 3;

t is an integer of from 0 to 2; and

u is an integer of from 0 to 1.

Other alpha2delta ligands that can be utilized in preferred embodiments of the invention methods are described, along with methods of synthesizing them, in United States Provisional Patent Application No. 60/368,413, filed on March 28, 2002. Such alpha2delta ligands are compounds of the formulas X, XA, XB, XI, XIA, XIB and XB-1, as described below, and their pharmaceutically acceptable salts.

Compounds of the formula X have the formula



X

wherein R_1 is hydrogen or $(C_1\text{-}C_3)$alkyl optionally substituted with from one to five fluorine atoms;

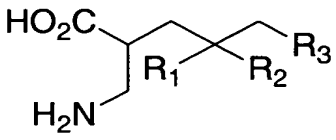
R_2 is hydrogen or $(C_1\text{-}C_3)$alkyl optionally substituted with from one to five fluorine atoms;

R_3 is $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl-$(C_1\text{-}C_3)$alkyl, phenyl, phenyl-$(C_1\text{-}C_3)$alkyl, pyridyl, pyridyl-$(C_1\text{-}C_3)$alkyl, phenyl-N(H)-, or pyridyl-N(H)- , wherein each of the foregoing alkyl moieties can be optionally substituted with from one to five fluorine atoms, preferably with from zero to three fluorine atoms, and wherein said phenyl and said pyridyl and the phenyl and pyridyl moieties of said phenyl-$(C_1\text{-}C_3)$alkyl and said pyridyl-$(C_1\text{-}C_3)$alkyl, respectively, can be optionally substituted with from one to three substituents, preferably with from zero to two substituents, independently selected from chloro, fluoro, amino, nitro, cyano, $(C_1\text{-}C_3)$alkylamino, $(C_1\text{-}C_3)$alkyl optionally substituted with from one to three

fluorine atoms and (C_1-C_3)alkoxy optionally substituted with from one to three fluorine atoms;

with the proviso that when R_1 is hydrogen, R_2 is not hydrogen.

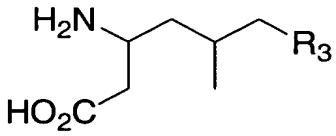
Compounds of the formula XI have the formula



XI

wherein R_1, R_2, and R_3 are defined as above in the definition of compounds of the formula X.

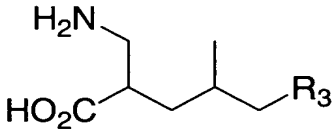
Compounds of the formula XA have the formula



XA

wherein R_3 is defined as above above in the definition of compounds of the formula X.

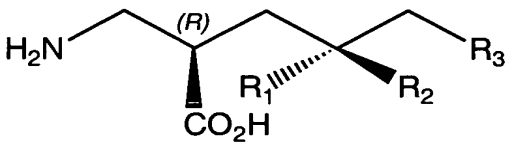
Compounds of the formula XIA have the formula



XIA

wherein R_3 is defined as above above in the definition of compounds of the formula X.

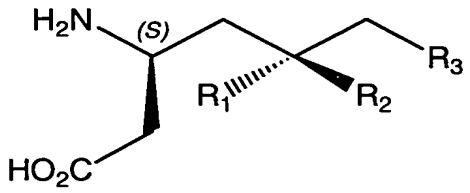
Compounds of the formula XIB have the formula



XIB

wherein R_1, R_2, and R_3 are defined as above above in the definition of compounds of the formula X.

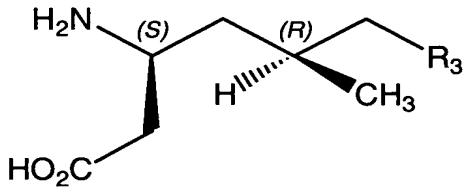
Compounds of the formula XB have the formula



XB

wherein R_1, R_2, and R_3 are defined as above above in the definition of compounds of the formula X.

Compounds of the formula XB-1 have the formula



XB-1

wherein R_3 is defined as above above in the definition of compounds of the formula X.

All U.S. patents and WO publications referenced above are incorporated herein by reference in their entireties.

It should be appreciated that the terms "uses", "utilizes", and "employs" are used interchangeably when describing an embodiment of the present invention.

The phrase "lower alkyl" means a straight or branched alkyl group or radical having from 1 to 6 carbon atoms, and includes methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *i*-butyl, *sec*-butyl, *tert*-butyl, *n*-pentyl, *n*-hexyl, and the like.

The term "alkyl", as used herein, unless otherwise indicated, includes saturated monovalent hydrocarbon radicals having straight, branched or cyclic moieties or combinations thereof. Examples of "alkyl" groups include, but are not limited to, methyl, ethyl, propyl, isopropyl, butyl, iso- sec- and tert-butyl, pentyl, hexyl, heptyl, 3-ethylbutyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, norbornyl, and the like.

The cycloalkyl groups are saturated monovalent carbocyclic groups containing from 3 to 8 carbons and are selected from cyclopropyl,

cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl, unless otherwise stated.

The benzyl and phenyl groups may be unsubstituted or substituted by from 1 to 3 substituents selected from hydroxy, amino, carboxy, carboalkoxy, halogen, CF_3, nitro, alkyl, and alkoxy. Preferred substituents are fluorine and chlorine.

Carboalkoxy is -COOalkyl wherein alkyl is as described above. Preferred carboalokoxy groups are carbomathoxy and carboethoxy.

The term "alkoxy", as used herein, unless otherwise indicated, means "alkyl-O-", wherein "alkyl" is as defined above. Examples of "alkoxy" groups include, but are not limited to, methoxy, ethoxy, propoxy, butoxy and pentoxy.

The term "alkenyl", as used herein, unless otherwise indicated, includes unsaturated hydrocarbon radicals having one or more double bonds connecting two carbon atoms, wherein said hydrocarbon radical may have straight, branched or cyclic moieties or combinations thereof. Examples of "alkenyl" groups include, but are not limited to, ethenyl, propenyl, butenyl, pentenyl, and dimethylpentyl, and include E and Z forms where applicable.

The term "aryl", as used herein, unless otherwise indicated, includes an aromatic ring system with no heteroatoms, which can be either unsubstituted or substituted with one, two or three substituents selected from the group consisting of halo, (C_1-C_4)alkyl optionally substituted with from one to three fluorine atoms and (C_1-C_4)alkoxy optionally substituted with from one to three fluorine atoms.

The term "aryloxy", as used herein, unless otherwise indicated, means "aryl-O-", wherein "aryl" is as defined above.

The term "heteroaryl", as used herein, unless otherwise indicated, includes an aromatic heterocycle containing five or six ring members, of which from 1 to 4 can be heteroatoms selected, independently, from N, S and O, and which rings can be unsubstituted, monosubstituted or disubstituted with substituents selected, independently, from the group

consisting of halo, (C_1-C_4)alkyl, and (C_1-C_4)alkoxy, optionally substituted with from one to three fluorine atoms.

The term "heteroaryloxy", as used herein, unless otherwise indicated, means "heteroaryl-O", wherein heteroaryl is as defined above.

The term "one or more substituents", as used herein, refers to a number of substituents that equals from one to the maximum number of substituents possible based on the number of available bonding sites.

The terms "halo" and "halogen", as used herein, unless otherwise indicated, include, fluoro, chloro, bromo and iodo.

The term "treating", as used herein, refers to reversing, alleviating, inhibiting the progress of, or preventing the disorder or condition to which such term applies, or preventing one or more symptoms of such condition or disorder. The term "treatment", as used herein, refers to the act of treating, as "treating" is defined immediately above.

The term "methylene", as used herein, means $-CH_2-$.

The term "ethylene", as used herein, means $-CH_2CH_2-$.

The term "propylene", as used herein, means $-CH_2CH_2CH_2-$.

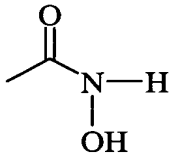
"Halogen" or "halo" includes fluorine, chlorine, bromine, and iodine.

Sulfonamides are those of formula $-NHSO_2R^{15}$ or $-SO_2NHR^{15}$ wherein R^{15} is a straight or branched alkyl group of from 1 to 6 carbons or a trifluoromethyl.

Amides are compounds of formula $-NHCOR^{12}$ wherein R^{12} is straight or branched alkyl of from 1 to 6 carbons, benzyl, and phenyl.

Phosphonic acids are $-PO_3H_2$.

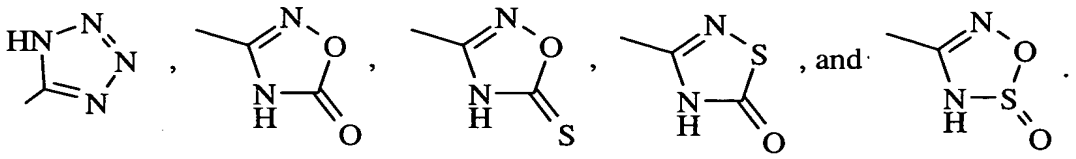
Sulfonic acids are $-SO_3H$.

Hydroxamic acid is  .

Heterocycles are groups of from 1 to 2 rings, the monocyclic rings having from 4 to 7 ring members and the bicyclic ring having from 7 to 12 ring members, wherein sucg rings contain from 1 to 6 heteroatoms

selected from oxygen, nitrogen, and sulfur, with the proviso that there are no two adjacent ring members that are oxygen.

Preferred heterocycles are



Compounds of formulas I – XI-B (*i.e.*, compounds of the formulas I, II, III, IV, V, VI, VII, VIII, IX, X, XA, XB, XB-1, XI, XIA, and XIB) may contain chiral centers and therefore may exist in different enantiomeric and diastereomeric forms. Individual isomers can be obtained by known methods, such as optical resolution, optically selective reaction, or chromatographic separation in the preparation of the final product or its intermediate. This invention relates to all optical isomers and all stereoisomers of compounds of the formulas I – XIB, both as racemic mixtures and as individual enantiomers and diastereoismers of such compounds, and mixtures thereof, and to all pharmaceutical compositions and methods of treatment defined above that contain or employ them, respectively. Individual enantiomers of the compounds of formula I may have advantages, as compared with the racemic mixtures of these compounds, in the treatment of various disorders or conditions.

In so far as the compounds of formulas I – XIB of this invention are basic compounds, they are all capable of forming a wide variety of different salts with various inorganic and organic acids. Although such salts must be pharmaceutically acceptable for administration to animals, it is often desirable in practice to initially isolate the base compound from the reaction mixture as a pharmaceutically unacceptable salt and then simply convert to the free base compound by treatment with an alkaline reagent and thereafter convert the free base to a pharmaceutically acceptable acid addition salt. The acid addition salts of the base compounds of this invention are readily prepared by treating the base compound with a substantially equivalent amount of the chosen mineral or organic acid in an aqueous solvent or in a suitable organic solvent, such as methanol or ethanol. Upon careful evaporation of the solvent, the desired solid salt is

readily obtained. The acids which are used to prepare the pharmaceutically acceptable acid addition salts of the aforementioned base compounds of this invention are those which form non-toxic acid addition salts, i.e., salts containing pharmaceutically acceptable anions, such as the hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate or bisulfate, phosphate or acid phosphate, acetate, lactate, citrate or acid citrate, tartrate or bi-tartrate, succinate, maleate, fumarate, gluconate, saccharate, benzoate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate and pamoate (i.e., 1,1'-methylene-bis-(2-hydroxy-3-naphthoate))salts.

The present invention also includes isotopically labelled compounds, which are identical to those recited in formulas I - XIB, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that can be incorporated into compounds of the present invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, sulfur, fluorine and chlorine, such as ^{2}H, ^{3}H, ^{13}C, ^{11}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, and ^{36}Cl, respectively. Compounds of the present invention, prodrugs thereof, and pharmaceutically acceptable salts of said compounds or of said prodrugs which contain the aforementioned isotopes and/or other isotopes of other atoms are within the scope of this invention. Certain isotopically labelled compounds of the present invention, for example those into which radioactive isotopes such as ^{3}H and ^{14}C are incorporated, are useful in drug and/or substrate tissue distribution assays. Tritiated, i.e., ^{3}H, and carbon-14, i.e., ^{14}C, isotopes are particularly preferred for their ease of preparation and detectability. Further, substitution with heavier isotopes such as deuterium, i.e., ^{2}H, can afford certain therapeutic advantages resulting from greater metabolic stability, for example increased *in vivo* half-life or reduced dosage requirements and, hence, may be preferred in some circumstances.

DETAILED DESCRIPTION OF THE INVENTION

The degree of binding to the α2δ subunit can be determined using the radioligand binding assay using [3H]gabapentin and the α2δ subunit derived from porcine brain tissue, as described by N. S. Gee *et al., J. Biol. Chem.*, 1996, *271*:5879-5776.

All that is required to practice the method of this invention is to administer an alpha2delta ligand, or a pharmaceutically acceptable salt thereof, in an amount that is therapeutically effective to treat one or more of the disorders or conditions referred to above. Such therapeutically effective amount will generally be from about 1 to about 300 mg/kg of subject body weight. Typical doses will be from about 10 to about 5000 mg/day for an adult subject of normal weight. In a clinical setting, regulatory agencies such as, for example, the Food and Drug Administration ("FDA") in the U.S. may require a particular therapeutically effective amount.

In determining what constitutes an effective amount or a therapeutically effective amount of an alpha2delta ligand, or a pharmaceutically acceptable salt thereof, for treating onr or more of the disorders or conditions referred to above according to the invention method, a number of factors will generally be considered by the medical practitioner or veterinarian in view of the experience of the medical practitioner or veterinarian, published clinical studies, the subject's age, sex, weight and general condition, as well as the type and extent of the disorder or condition being treated, and the use of other medications, if any, by the subject. As such, the administered dose may fall within the ranges or concentrations recited above, or may vary outside, *i.e.,* either below or above, those ranges depending upon the requirements of the individual subject, the severity of the condition being treated, and the particular therapeutic formulation being employed. Determination of a proper dose for a particular situation is within the skill of the medical or veterinary arts. Generally, treatment may be initiated using smaller dosages of the alpha2delta ligand that are less than optimum for a particular subject. Thereafter, the dosage can be increased by small increments until the optimum effect under the circumstance is reached.

For convenience, the total daily dosage may be divided and administered in portions during the day, if desired.

Pharmaceutical compositions of an alpha2delta ligand, or a pharmaceutically acceptable salt thereof, are produced by formulating the active compound in dosage unit form with a pharmaceutical carrier. Some examples of dosage unit forms are tablets, capsules, pills, powders, aqueous and nonaqueous oral solutions and suspensions, and parenteral solutions packaged in containers containing either one or some larger number of dosage units and capable of being subdivided into individual doses.

Some examples of suitable pharmaceutical carriers, including pharmaceutical diluents, are gelatin capsules; sugars such as lactose and sucrose; starches such as corn starch and potato starch; cellulose derivatives such as sodium carboxymethyl cellulose, ethyl cellulose, methyl cellulose, and cellulose acetate phthalate; gelatin; talc; stearic acid; magnesium stearate; vegetable oils such as peanut oil, cottonseed oil, sesame oil, olive oil, corn oil, and oil of theobroma; propylene glycol, glycerin; sorbitol; polyethylene glycol; water; agar; alginic acid; isotonic saline, and phosphate buffer solutions; as well as other compatible substances normally used in pharmaceutical formulations.

The compositions to be employed in the invention can also contain other components such as coloring agents, flavoring agents, and/or preservatives. These materials, if present, are usually used in relatively small amounts. The compositions can, if desired, also contain other therapeutic agents commonly employed to treat the disorder or condition being treated.

The percentage of the active ingredients in the foregoing compositions can be varied within wide limits, but for practical purposes it is preferably present in a concentration of at least 10% in a solid composition and at least 2% in a primary liquid composition. The most satisfactory compositions are those in which a much higher proportion of the active ingredient is present, for example, up to about 95%.

Preferred routes of administration of an alpha2delta ligand, or a pharmaceutically acceptable salt thereof, are oral or parenteral. For example, a useful intravenous dose is between 5 and 50 mg, and a useful oral dosage is between 20 and 800 mg.

The alpha2delta ligand, or a pharmaceutically acceptable salt thereof, may be administered in any form. Preferably, administration is in unit dosage form. A unit dosage form of the alpha2delta ligand, or a pharmaceutically acceptable salt thereof, to be used in this invention may also comprise other compounds useful in the therapy of the disorder or condition for which the alpha2delta ligand is being administered or a disorder or condition that is secondary to the disorder or treatment for which the alpha2delta ligand is being administered.

Some of the compounds utilized in a method of the present invention are capable of further forming pharmaceutically acceptable salts, including, but not limited to, acid addition and/or base salts. The acid addition salts are formed from basic compounds, whereas the base addition salts are formed from acidic compounds. All of these forms are within the scope of the compounds useful in the method of the present invention.

Pharmaceutically acceptable acid addition salts of the basic compounds useful in the method of the present invention include nontoxic salts derived from inorganic acids such as hydrochloric, nitric, phosphoric, sulfuric, hydrobromic, hydroiodic, hydrofluoric, phosphorous, and the like, as well nontoxic salts derived from organic acids, such as aliphatic mono- and dicarboxylic acids, phenyl-substituted alkanoic acids, hydroxy alkanoic acids, alkanedioic acids, aromatic acids, aliphatic and aromatic sulfonic acids, etc. Such salts thus include sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, nitrate, phosphate, monohydrogenphosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, chloride, bromide, iodide, acetate, trifluoroacetate, propionate, caprylate, isobutyrate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, mandelate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, phthalate, benzenesulfonate, toluenesulfonate, phenylacetate, citrate, lactate,

malate, tartrate, methanesulfonate, and the like. Also contemplated are salts of amino acids such as arginate and the like and gluconate, galacturonate (see, for example, Berge S.M. et al., "Pharmaceutical Salts," *J. of Pharma. Sci.*, 1977;66:1).

An acid addition salt of a basic compound useful in the method of the present invention is prepared by contacting the free base form of the compound with a sufficient amount of a desired acid to produce a nontoxic salt in the conventional manner. The free base form of the compound may be regenerated by contacting the acid addition salt so formed with a base, and isolating the free base form of the compound in the conventional manner. The free base forms of compounds prepared according to a process of the present invention differ from their respective acid addition salt forms somewhat in certain physical properties such as solubility, crystal structure, hygroscopicity, and the like, but otherwise free base forms of the compounds and their respective acid addition salt forms are equivalent for purposes of the present invention.

A pharmaceutically acceptable base addition salt of an acidic compound useful in the method of the present invention may be prepared by contacting the free acid form of the compound with a nontoxic metal cation such as an alkali or alkaline earth metal cation, or an amine, especially an organic amine. Examples of suitable metal cations include sodium cation (Na^+), potassium cation (K^+), magnesium cation (Mg^{2+}), calcium cation (Ca^{2+}), and the like. Examples of suitable amines are N,N′-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, dicyclohexylamine, ethylenediamine, N-methylglucamine, and procaine (see, for example, Berge, supra., 1977).

A base addition salt of an acidic compound useful in the method of the present invention may be prepared by contacting the free acid form of the compound with a sufficient amount of a desired base to produce the salt in the conventional manner. The free acid form of the compound may be regenerated by contacting the salt form so formed with an acid, and isolating the free acid of the compound in the conventional manner. The free acid forms of the compounds useful in the method of the present

invention differ from their respective salt forms somewhat in certain physical properties such as solubility, crystal structure, hygroscopicity, and the like, but otherwise the salts are equivalent to their respective free acid for purposes of the present invention.

Certain of the compounds useful in the method of the present invention can exist in unsolvated forms as well as solvated forms, including hydrated forms. In general, the solvated forms, including hydrated forms, are equivalent to unsolvated forms and are intended to be encompassed within the scope of the present invention.

Certain of the compounds useful in the method of the present invention possess one or more chiral centers, and each center may exist in the R or S configuration. A method of the present invention may utilize any diastereomeric, enantiomeric, or epimeric form of an alpha2delta ligand, or a pharmaceutically acceptable salt thereof, as well as mixtures thereof.

Additionally, certain compounds useful in the method of the present invention may exist as geometric isomers such as the entgegen (E) and zusammen (Z) isomers of alkenyl groups. A method of the present invention may utilize any cis, trans, syn, anti, entgegen (E), or zusammen (Z) isomer of an alpha2delta ligand, or a pharmaceutically acceptable salt thereof, as well as mixtures thereof.

Certain compounds useful in the method of the present invention can exist as two or more tautomeric forms. Tautomeric forms of the compounds may interchange, for example, via enolization/de-enolization and the like. A method of the present invention may utilize any tautomeric form of an alpha2delta ligand, or a pharmaceutically acceptable salt thereof, as well as mixtures thereof.

The following examples illustrate the invention pharmaceutical compositions containing an alpha2delta ligand, and a pharmaceutically acceptable carrier, diluent, or excipient. The examples are representative only, and are not to be construed as limiting the invention in any respect.

FORMULATION EXAMPLE 1

Tablet Formulation:

Ingredient	Amount (mg)
3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride	25
Lactose	50
Cornstarch (for mix)	10
Cornstarch (paste)	10
Magnesium stearate (1%)	5
Total	100

3-(1-Aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride, lactose, and cornstarch (for mix) are blended to uniformity. The cornstarch (for paste) is suspended in 200 mL of water and heated with stirring to form a paste. The paste is used to granulate the mixed powders. The wet granules are passed through a No. 8 hand screen and dried at 80°C. The dry granules are lubricated with the 1% magnesium stearate and pressed into a tablet. Such tablets can be administered to a human from one to four times a day for treatment of ADHD.

FORMULATION EXAMPLE 2

Coated Tablets:

The tablets of Formulation Example 1 are coated in a customary manner with a coating of sucrose, potato starch, talc, tragacanth, and colorant.

FORMULATION EXAMPLE 3

Injection vials:

The pH of a solution of 500 g of gabapentin and 5 g of disodium hydrogen phosphate is adjusted to pH 6.5 in 3 L of double-distilled water using 2 M hydrochloric acid. The solution is sterile filtered, and the filtrate is filled into injection vials, lyophilized under sterile conditions, and aseptically sealed. Each injection vial contains 25 mg of gabapentin.

FORMULATION EXAMPLE 4

Suppositories:

A mixture of 25 g of (1α,3α,5α)(3-aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid hydrochloride, 100 g of soya lecithin, and 1400 g of cocoa butter is fused, poured into molds, and allowed to cool. Each suppository contains 25 mg of (1α,3α,5α)(3-aminomethyl-bicyclo[3.2.0]hept-3-yl)-acetic acid hydrochloride.

FORMULATION EXAMPLE 5

Solution:

A solution is prepared from 1 g of 3-(2-aminomethyl-4-methyl-pentyl)-4H-[1,2,4]-oxadiazol-5-one hydrochloride, 9.38 g of $NaH_2PO_4 \cdot 12H_2O$, 28.48 g of $Na_2HPO_4 \cdot 12H_2O$, and 0.1 g benzalkonium chloride in 940 mL of double-distilled water. The pH of the solution is adjusted to pH 6.8 using 2 M hydrochloric acid. The solution is diluted to 1.0 L with double-distilled water, and sterilized by irradiation. A 25 mL volume of the solution contains 25 mg of 3-(2-aminomethyl-4-methyl-pentyl)-4H-[1,2,4]-oxadiazol-5-one hydrochloride.

FORMULATION EXAMPLE 6

Ointment:

500 mg of 3-(1-aminomethyl-cycloheptylmethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride is mixed with 99.5 g of petroleum jelly under aseptic conditions. A 5 g portion of the ointment contains 25 mg of 3-(1-aminomethyl-cycloheptylmethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride.

FORMULATION EXAMPLE 7

Capsules:

2 kg of 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride are filled into hard gelatin capsules in a customary manner such that each capsule contains 25 mg of 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one hydrochloride.

FORMULATION EXAMPLE 8

Ampoules:

A solution of 2.5 kg of gabapentin is dissolved in 60 L of double-distilled water. The solution is sterile filtered, and the filtrate is filled into ampoules. The ampoules are lyophilized under st erile conditions and aseptically sealed. Each ampoule contains 25 mg of gabapentin.

Having described the invention method, various embodiments of the invention are hereupon claimed.